CARDIOPULMONARY FUNCTION IN YOUTH

KENNETH F. CRUMLEY

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CARDIOPULMONARY FUNCTION IN YOUTH:

Rise in Respiratory Exchange Ratio

During Exercise As a Metabolic Measure

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Contents

Many thanks are due to Dr. Norman Talner for this research opportunity and for his advice and encouragement; to Dr. Guy Rivard for his cheerful pessimism, his critical eye, and his invaluable guidance; to Dorothy Nixon for her photographic mastery; and to Carol Masotta for her unerring typistry.

PARENTIBUS OPTIMIS

"This being of mine, whatever it be, consists of a little flesh, a little breath, and the part which governs."

Marcus Aurelius, Meditations

Introduction

The aim of this research has been to select and study a method for the evaluation of total cardiopulmonary function in children and adolescents which would be reliable, technically simple, and easily reproducible. These stipulations necessitate a minimum number of measurements and a painless and unexhausting experience for the subject.

The method chosen has been described by Wasserman (1) and uses exercise to assess the circulatory and pulmonary function of supplying oxygen to the working muscles. The status of the heart and lungs as a unit will be reflected by their ability to perform this function. The subject exercises on a bicycle ergometer at gradually increasing work loads. Percentages of CO_2 and N_2 in the expired air are analyzed breath-by-breath and are used to calculate the respiratory quotient. The point on the work scale at which the R.Q. rises significantly is taken to represent the "threshold of anaerobic metabolism" (1), the point at which the cardiopulmonary system can no longer keep pace with oxygen demand. This "threshold" appears at a submaximal load and thus avoids the problems associated with pushing the subject to maximal performance. The method is not designed to discriminate among different disease processes or states but rather to determine over-all function regardless of the presence or absence of disease.

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It has been our purpose to use this method to establish ranges of cardiopulmonary efficiency for normal children of various ages, sizes, and habits, then to compare these with those of patients with cardiac or pulmonary disease.

First, we will consider the process of selecting a method which fits the criteria established. The theory of the method and its application will be discussed. Finally, we will compare our results with those of previous exercise studies in children, then assess the possibilities of the method under study.

Section I - Physiological Responses to Exercise

During exercise, various components of cardiopulmonary function undergo changes. These include changes in circulatory mechanisms, ventilation, body temperature regulation, and metabolism. Some of these functions are more accurate indicators of physical working capacity and can be measured more easily than others. The search for the ideal method of assessing cardiopulmonary capacity in children requires that one carefully evaluate these aspects of the physiology of exercise in order to determine the most suitable measurements. We will review exercise under these four general headings and discuss the relative merits of the possible measurements.

Changes in Circulation

With exercise, changes occur in various circulatory functions which may be measured to give an idea of how much the circulation is taxed by a particular work load. Cardiac output and blood pressure increase, heart rate rises, and electrocardiographic changes are observed.

The increased metabolic needs of the muscles engaged in exercise are met by an increased oxygen uptake, which depends upon increases in cardiac output and tissue oxygen removal. The Fick equation defines the relationship of oxygen uptake ($\mathring{V}_{O_2}$) to cardiac output ($\mathring{Q}$) and arteriovenous

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oxygen difference (equal to tissue oxygen removal) as:

$$\mathring{V}_{O_2} = \mathring{Q} \times (\text{A-V } O_2 \text{ difference})$$

Thus oxygen uptake increases as do the two factors upon which it depends (3). It has been shown by Asmussen and Nielsen (2) that oxygen uptake and cardiac output are almost rectilinearly related. Therefore, since the resultant increase in blood flow is shunted mostly to the large muscle groups, and since O_2 uptake is a good indicator of aerobic working capacity (see next section on Metabolism), cardiac output increase is thought to be directly related to working capacity. Methods for determining cardiac output (e.g. the direct Fick method and the indicator dilution technique), however, are difficult and therefore impractical as tests where speed and simplicity are important.

Since cardiac output is the product of stroke volume and heart rate, one of these two determinants might provide the index needed. The stroke volume may be measured as a separate entity. Some investigators report no change or only slight changes in stroke volume in light exercise. The central venous volume is higher supine than standing (3). So, if the resting value for stroke volume is determined lying down, the changes with upright exercise are small. But if the resting value is obtained with the subject sitting or standing, there is a significant increase even at low work loads (4).

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Since cardiac output is the product of stroke volume and heart rate, one of these two determinants might provide the index needed. The stroke volume may be measured as a separate entity. Some investigators report no change or only slight changes in stroke volume in light exercise. The maximal stroke volume is highly greater than resting volume. So, if the resting value of the stroke volume is determined lying down, the changes with upright exercise are small. But if the resting value is obtained with the subject sitting or standing, there is a substantial increase even with moderate loads (1).

Chapman et al. (5) found that the stroke volume increased with increasing exercise levels but concluded that the relationship is probably not linear. In their opinion from one-third to one-half the rise in cardiac output from resting level (7.2 L/Min.) to near the maximum oxygen intake level (21.9 L/Min.) is attributable to increase in stroke volume.

According to Åstrand (6), the maximum stroke volume is reached at a work load corresponding to an oxygen uptake of 40 percent of maximum and to a heart rate of about 110. He found that in females the stroke volume increased on the average from 68 ml. to 100 ml. (rest to maximum value) and in males from 88 ml. to 134 ml., an increase of about 50 percent. Maximum stroke volume conceivably could be used as an indicator of aerobic capacity, were its measurement not so difficult.

Heart rate correlates better than stroke volume with working capacity and has been used extensively in testing. Heart rate rises when exercise begins and reaches a steady value in a few minutes if the work load is maintained (3). There is a rectilinear relationship between oxygen uptake and pulse rate up to maximal O_2 uptake (7). Since physical training increases O_2 uptake for any particular pulse rate, this rate will be lower for a given work load in the athlete than in the non-athlete (8).

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Rushmer and Smith (9) found that, while the most reliable measurements of cardiorespiratory function during exercise are cardiac output and oxygen consumption, there is a high correlation between pulse rate and O_2 consumption. They considered a pulse rate of 170 to represent about 80 percent of maximal O_2 consumption.

Sjöstrand (10) and Åstrand (11,12) found that pulse rate increased rectilinearly with work load as measured on a bicycle ergometer. They showed that when the load was increased, a new steady state could be reached in three to five minutes. Sjöstrand (10) defined "working capacity" as that amount of work necessary to increase the heart rate to 170. Several studies have been done in children, taking the work load achieved at a rate of 170 to represent working capacity, including those of Bengtsson (13), Cumming (14), and Adams, (15,16).

While a near maximal pulse rate is a good measurement of cardiopulmonary capacity, one essential criterion of the ideal method is that the test be a submaximal one. A maximal effort may be dangerous for a child with cardiac or pulmonary disease. Also, it is difficult for even a normal child to achieve a maximal effort, as an element of will is involved. Since the relation between pulse rate and working capacity is apparently linear, it seems logical that extrapolation from a submaximal pulse rate to 170 would yield

the true working capacity. According to Friesen et al. (63), however, this extrapolation yields a falsely high estimate of the working capacity.

Systolic, diastolic, and mean arterial blood pressures rise with exercise, reaching after several minutes steady levels which are higher with more strenuous work and higher at a given intensity in an untrained subject than in a trained one. The lower pressures in a trained individual are most likely due to decreased peripheral resistance (3).

There are also electrocardiographic changes in exercise. Normal changes as studied by Bellet et al. (18) include sinus tachycardia, increased amplitude of the P wave, junctional S-T segment depression, and diminished (68%) or increased (17%) amplitude of the T wave at a pulse rate of about 140. Changes in the electrocardiogram and the blood pressure are thus very rough indices of work intensity.

Changes in Ventilation

Greater oxygen requirements and accumulation of metabolic products in exercise necessitate an increase in pulmonary ventilation. This ventilatory response seems to be the result of a combination of influences, some neurogenic (central response and peripheral mechanoreceptors), some humoral (changes in CO_2, $H+$, O_2 and catecholamines). But the importance of each factor is not known at the present time (3).

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Changes in Testosterone

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There is an increase in both respiratory depth and frequency with exercise. In light work the change is mainly in depth; respiratory rate rises as exercise becomes heavier. Tidal volumes may approach 50 percent of the vital capacity; respiratory frequency may increase to as much as 40 to 50 breaths per minute in adults (from a resting frequency of about 20) and to 70 in children (3,19).

It has been shown that hyperpnea in exercise closely parallels the rise in O_2 uptake up to a certain point (3). Asmussen (17) found that, as arterial lactic acid concentration rises above resting level, ventilation starts to increase more rapidly than oxygen uptake. Thus changes in ventilation may give some idea of the aerobic capacity.

On the other hand, there are factors which limit the reliability of the parameters of ventilation as measurements of the working capacity. First, maximum respiratory frequency varies from person to person and cannot really be standardized. Also, if the exercise is rhythmic and the sequence of movements regular (especially in the case of riding a bicycle), the subject may tend to breathe in time with the movements, and respiration may be faster or slower than the rate set by oxygen need (3).

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<u>Changes in Body Temperature</u>

Body heat, at rest, is created by the combustion of breakdown products of foodstuffs by the cells. Carbohydrates, fats and proteins are metabolized to produce energy for work, and some of the energy released is converted to heat. Body temperature reflects a balance of heat production and heat dissipation; heat loss is mainly through the skin (3).

Body temperature rises significantly in muscular exercise. Of the energy produced in exercise above the basal metabolic production, about 75 percent is converted to heat and only 25 percent to work. At the same time the blood flow to the skin is reduced since more of the cardiac output is diverted to the muscles. Thus, heat accumulates in the body. The amount of rise in temperature depends on the work intensity and the conditions in the ambient air (excessive heat and humidity reduce heat loss). The rise is slow and levels off after 30 to 60 minutes of work; the temperature remains elevated for 45 to 60 minutes after cessation of work (3).

Since temperature rises in rectilinear fashion with work intensity, it is possible that higher temperatures may correlate with higher working capacity. It is known that heat speeds up molecular movement, causing a swifter exchange of metabolites; also, heat increases tissue oxygen supply

by shifting the oxygen dissociation curve of hemoglobin to the right (3). Åstrand (20) showed, by determining maximum working capacity, that performance in activities such as bicycling, running, and swimming is improved in proportion to increase in body temperature. Unfortunately, temperature rise is slow enough that it cannot be an accurate indicator in a test of short duration.

<u>Changes in Metabolism</u>

During exercise the muscles require energy for contraction and the performance of work. This energy is supplied by the oxidative degradation of carbohydrate, fat, and protein. The oxygen requirement for these biochemical processes (above the basal metabolic requirement) is thus a measure of work performed (3).

There is a small amount of oxygen stored in the body which may be used to perform work of short duration. This oxygen is stored in red cells in combination with hemoglobin and in muscle combined with myoglobin (3). Åstrand (20) reported that a great amount of work can be done with a submaximal load on the circulation and respiration by alternating short work periods with short rest periods (with a 1:1 time ratio). As a possible explanation he offered this storage of oxygen in myoglobin and hemoglobin; he suggested that myoglobin may function as an oxygen store for the initial

phase of work before the circulation and respiration can meet the increased oxygen demand.

Since these blood and tissue stores amount to only about one liter of oxygen, for longer exercise periods, oxygen intake must parallel work output. Therefore, except for short periods, and for periods when work load is being increased, alveolar oxygen uptake is an accurate index of oxygen used for energy production.

The length of time necessary for cardiorespiratory adaptation to increased oxygen need depends upon the intensity of the exercise. In very strenuous exercise oxygen uptake may not reach a steady state for 5 to 10 minutes.

Maximal O_2 uptake depends upon age, sex, body surface area, and physical fitness. Training can increase the oxygen uptake significantly, largely by increasing the O_2 transporting capacity of the cardiopulmonary system. Conditioning may also influence the capacity of muscle tissue for extracting oxygen from the blood (3). Åstrand (21) defines maximal oxygen intake as "aerobic capacity" and suggests that in work with large groups of muscles the limiting factor is the capacity and regulation of the oxygen transportation system. Åstrand (22) also writes: "The measurement of maximal oxygen uptake of a subject in muscular exercise gives the maximal rate of energy output by combustion within the body. If we assume that cardiac output increases linearly with oxygen uptake, then maximal oxygen uptake indicates the function of the heart and circulation".

Chapman et al. (23) stressed the contribution of local tissue factors in increasing the maximal oxygen intake. In fifteen normal subjects they found that the O_2 intake was increased 9.5 times at maximal intake over the resting value. Cardiac output was increased 4.3 times, pulse and stroke volume 2 times. Rise in cardiac output permitted O_2 intake to increase from 340 ml. to 1500 ml. Widening of the arteriovenous oxygen difference 2.2 times, however, permitted an increase to 3 liters (mixed venous oxygen content fell from 11.6 ml./100 ml. to 5.0 ml./100 ml.); this was attributed to increased tissue O_2 extraction and to the shunting of blood away from inactive areas.

The investigators in this area agree with Taylor et al. (24) who found that, when a large proportion of the body muscle mass is engaged in work, there is a straight-line relation between O_2 uptake and work load up to maximal O_2 uptake, and that consequently the maximal O_2 intake is a good objective measurement of cardiorespiratory performance.

Unfortunately, there are two aspects to this measurement which make it unsuitable for the purposes stated. In the first place, the methods for measuring O_2 uptake during exercise are somewhat complicated; the subject breathes into a mask or mouthpiece; expired air is collected in Douglas bags and then analyzed with gas analyzers of the Haldane or Scholander type. More importantly, this test requires a maximum effort, which may be dangerous for persons

with significant disease, and which calls for high motivation from all subjects.

Study of other metabolic phenomena, however, has shown the way to the development of an important method for assessing cardiopulmonary function at submaximal exercise levels. In strenuous muscular exercise, the most important pathway of substrate oxidation for energy production is the Embden-Meyerhof glycolytic pathway, which involves the breakdown of glycogen or glucose to pyruvate and lactate. This pathway provides substrate for further oxidation in the Krebs cycle and provides a supply of energy under conditions in which oxygen supply is low (e.g. in very strenuous muscular exercise). When O_2 tension is normal and when the energy demand is basal or moderate, the largest part of the pyruvic acid formed in glycolysis is oxidized to acetyl-CoA which enters the citric acid cycle. When oxygen tension is low or oxygen demand very high, more pyruvate is produced than can be transformed by oxidation, and this excess pyruvate forms lactic acid (25).

This reaction leading to production of lactic acid balances the oxidation-reduction system. Because of this situation, glycolysis can continue to provide energy for work in the form of "high-energy" phosphate bonds even when oxygen supply cannot meet demand. During hypoxia, glycolysis produces either two or three "high-energy" bonds; glu-

cose oxidation by glycolysis and the Krebs cycle will yield 36 bonds when oxygen supply is normal (25).

When oxygen supply fails to meet demand, an "oxygen debt" is contracted. The amount of the oxygen debt is equal to the oxygen uptake, during recovery from exercise, which is in excess of the resting value (3). There has been some dispute concerning the identity of the creditors for the debt. According to Huckabee (26), oxygen debt formation represents a need for oxygen during exercise which is satisfied only during recovery and is approximated by the amount of "excess lactate" formed (this quantity indicates amount of lactate formed during anaerobic metabolism in excess of the amount of pyruvate obtained from the pyruvate $\rightleftharpoons$ lactate reaction). Knuttgen (27) also attributes the oxygen debt completely to excess lactate which he finds appears at all levels of exercise.

Other workers (28) have found that an oxygen debt of up to 1.5 to 2.0 liters of O_2 may exist without appreciable increase in lactate. Margaria (29) feels that early in exercise there is an anaerobic process which is "alactacid", and that later all the energy liberated is accounted for by combustion processes plus lactate formation from glycogen (contraction of the "lactacid" O_2 debt). The "alactacid" debt is thought to be paid to the energy sources which are important at the beginning of exercise before cardiorespiratory

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adaptation is complete, (e.g. high-energy phosphate bonds), and to the oxygen sources oxyhemoglobin and oxymyoglobin (3).

Dill (30) found the O_2 consumption curve during recovery to be the sum of four functions: 1) basal O_2 consumption, 2) O_2 consumption attributed to the oxidation of lactic acid, 3) payment of the alactacid debt (this taking place 30 times as fast as the 2nd function), and 4) a very slow component (because of this last, O_2 consumption may remain 10 to 20 percent above basal levels after several hours).

The consensus is that in fairly strenuous exercise, when muscle metabolic processes become partly anaerobic, lactic acid is produced and diffuses into the blood. Below a certain work load, lactate concentration remains close to the resting value. At the point when oxygen supply fails below demand, lactate concentration rises precipitously (3).

Wells et al. (31) classified work levels in adults according to the amount of lactic acid accumulation. In their study, light work occurs at a pulse rate of 120 or less and involves no lactate rise above the resting level. Heavy work implies a pulse rate of 120 to 160 and an increase in lactate of 20 to 40 mg. percent. In severe exercise the pulse rate exceeds 160 and lactate rise may approach 100 mg. percent. The point at which lactate began to exceed resting levels was thought by Wells (31) to correspond to a level of per-

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formance which was about 50 percent of the working capacity.

Because of the relatively high dissociation constant of lactic acid, it is virtually all ionized in the physiologic pH range. Thus, after diffusing into the blood, lactic acid is completely buffered (32). According to Turrell and Robinson (33), increased lactic acid up to 4 mEq/L is buffered mainly by sodium bicarbonate with the formation of sodium lactate, H_2O and CO_2; above this level plasma proteins and hemoglobin begin to account for more of the needed base.

Harrison and Pilcher (34) first discovered that patients in heart failure produced more carbon dioxide than normal subjects doing the same exercise. This increased the respiratory exchange ratio R (defined as CO_2 production/O_2 consumption). They concluded that the excess CO_2 was formed as bicarbonate buffered lactic acid. Although Harrison and Pilcher detected no significant increases in R in normals at the low loads which they studied, metabolic acidosis does develop in normal subjects at higher loads and R rises (32) (see Fig. 1).

Issekutz (35) first used the respiratory exchange ratio (equal to the metabolic respiratory quotient in the steady state) as an index of anaerobic metabolism. He found that the rise in R seemed to depend on intensity of work and that, in heavy work, R was always greater than 1.0 and often

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Issekutz (15) (1962) used the respiratory exchange ratio (equal to the metabolic respiratory quotient in the steady state) as an index of anaerobic metabolism. He found that the rise in R seemed to depend on intensity of work and that, in heavy work, R was always greater than 1.0 and often

reached 1.2 or more. He found that excess CO_2 (total CO_2 - 0.75 x O_2 consumption, where 0.75 is an assumed resting R.Q.) rose initially, fell, then rose again. These changes correlated with blood lactate changes. He explained the initial increase in R as due to discrepancy between oxygen supply and demand. The second rise in R was taken to represent the percent participation of anaerobic glycolysis rather than the fuel used for work. Issekutz concluded that since lactic acid concentration is higher in working muscle than in blood, and since diffusion of "bicarbonate CO_2" is presumably more rapid than that of lactate, excess CO_2 may follow anaerobic metabolism more closely than blood lactate level.

Naimark, Wasserman, and McIlroy employed these concepts to develop a simple method of evaluating cardiopulmonary function by continuous measurement of R. In their first paper (36) they found, with increasing work intensity, the development of metabolic acidosis (simultaneous rise in lactic acid and R, and fall in pH and bicarbonate)(Fig. 2). They used rapidly responding nitrogen and carbon dioxide analyzers to measure breath-by-breath R with increasing work loads (R can be calculated from alveolar N_2 and CO_2 by an equation derived from the alveolar gas equations; see analysis of data under Material and Methods). They affirmed that the rise in R was not due to hyperventilation, as alveolar and arterial pCO_2 did not decrease. They also determined

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that the load corresponding to the increase in R was constant for a given individual; depending mainly on physical fitness and type of exercise.

In the second study, Naimark et al. (37) again found close correlation between the rise in lactic acid and R and the fall in pH and bicarbonate. They obtained a curve, by plotting Δ R vs. O_2 consumption, which was roughly sigmoid (see Fig. 6), consisting of an initial slow rise, a steep rise, and a further slow rise.

Wasserman and McIlroy (1) used this method to evaluate cardiopulmonary status in cardiac patients. By plotting R vs. O_2 consumption, they obtained sigmoid curves similar to those of Naimark et al. (37) and to those of Issekutz (38). Wasserman and McIlroy (36) postulated that the steepest part of the curve indicated the level of oxygen consumption at which anaerobic metabolism becomes important, and termed it the "threshold of anaerobic metabolism".

Wasserman et al. (39) tested ten subjects at three different work levels on a bicycle ergometer and found that below the work level representing the anaerobic threshold the subjects could exercise for long periods (50 min. in this case) in a steady state without developing a metabolic acidosis.

Wasserman et al. (40) further defined the anaerobic threshold as a specific load below which, in a normal subject, there exists a cardiorespiratory reserve. They found

that the load corresponding to the increase in [illegible] was constant for a given individual, depending mainly on physical fitness and type of exercise.

In the second study, Wasserman et al. [illegible] again found close correlation between the rise in lactic acid [illegible] and the fall in pH and bicarbonate. They proposed a theory, hypothesizing [illegible] consumption [illegible] model (see Fig. [illegible]) [illegible] steep rise, and a [illegible] rise.

Wasserman and McIlroy [illegible] cardiopulmonary disease in cardiac patients. By [illegible] vs. $\dot{V}_{O_2}$ consumption, they obtained [illegible] similar to those of [illegible] et al. [illegible] and to those of [illegible]. Wasserman and McIlroy [illegible] concluded that the [illegible] of the [illegible] indicated the onset of [illegible] at which anaerobic metabolism [illegible] the "threshold of anaerobic metabolism".

Wasserman et al. [illegible] [illegible] work [illegible] and found that [illegible] low [illegible] the [illegible] subjects could [illegible] in a steady state [illegible] [illegible].

Wasserman et al. [illegible] [illegible] threshold [illegible] in a normal subject [illegible] [illegible].

no metabolic acidosis or increase in arterial blood lactate until the energy requirement reached four times the basal level. Thus the anaerobic threshold during exercise reflects the oxidative balance of the subject as a whole. Specific muscle groups may produce lactic acid at "subthreshold" loads, but this will be compensated by other tissues.

From all indications the method elaborated by Issekutz and developed by Naimark, Wasserman, and McIlroy represents possibly an ideal way to evaluate carefully the cardio-respiratory function. The procedure is relatively simple, involves no trauma (e.g. drawing blood), and need not be carried to the point of exhaustion.

One further question concerns which specific exercise test to use. The step test designed by Master (41) has been long used, especially to detect coronary artery insufficiency. In exercise with this test it is difficult to make measurements; also, only one level of work can be performed, and extrapolation to a maximal level is not possible.

The treadmill has been widely used in testing exercise fitness and has certain advantages. Only the ability to walk is required, and numerous gradations of exercise can be achieved. Disadvantages of the treadmill are its bulkiness and expense (42).

The bicycle ergometer fits the criteria suggested by Rodahl (43) for an optimal measurement of physical fitness. First, large muscle groups are used. Taylor et al. (24) found that maximal oxygen intake increases with the amount of muscle mass employed. Later Asmussen and Hemmingsen (44) reported, in normals, a greater aerobic capacity in leg work than in arm work. Duner (45) found that working capacity with one leg was 73 to 80 percent of that using both legs. Also, according to Åstrand (64), aerobic capacity and maximal heart rate are not different in maximal running and cycling from cranking plus cycling or from those measurements in very strenuous activities, such as skiing and swimming.

Other criteria (43) met by the bicycle (42) are that the work load be measurable and adjustable, and that results be comparable for a given individual under different conditions and between individuals. The adjustable seat allows constant mechanical efficiency for both trained and untrained subjects (43). Also Rodahl (43) showed that, at a given load, a steady state is reached between the third and fifth minute of work for pulmonary ventilation, oxygen uptake and pulse rate. The bicycle requires only a minimum of skill and is very familiar to most healthy children.

The bicycle ergometer (the one initially suggested by Kodahl (46)) has an optimal measurement of physical fitness, since large muscle groups are used. Taylor et al. (61) found that maximal oxygen intake increased with the amount of muscle mass employed. [illegible] and [illegible] (44) reported, in general, a greater aerobic capacity in leg work than in arm work. Asmussen (4) found that working capacity with one leg was 75 to 80 percent of that using both legs. Also, according to [illegible] (10), maximal oxygen uptake [illegible] that are not different in maximal [illegible] and cycling from treadmill [illegible] to from these measurements in very strenuous conditions, such as [illegible] and [illegible].

Other criteria (11) set up the [illegible] (17) are that the work load be reproducible and [illegible], and that results be comparable for a given individual under different conditions and between individuals. The bicycle ergometer allows constant mechanical efficiency for both trained and untrained subjects (43). [illegible] (47) showed that, at a given load, a steady state is reached between the [illegible] minute of work for pulmonary ventilation, oxygen uptake and heart rate. The bicycle requires only a minimum of skill and is easy to [illegible] or [illegible].

Section II - Material and Methods

Population

Studies were done on 95 subjects aged 6 to 20 years - 65 normals and 30 children with significant disease, including 62 males and 33 females, 84 whites and 11 Negroes. Normals were drawn from the General Pediatric Clinic of the Yale-New Haven Hospital (these were well children who were in the clinic for a routine physical checkup or were relatives or friends accompanying sick children), from among the laboratory technician and secretary population, and from the local community. Patients were taken from the General Pediatric Clinic and from the Pediatric Cardiac Clinic. All participants were questioned closely about their past medical history in order to determine the presence or absence of disease. Documented past history was reviewed when available.

Procedure

First, an information sheet was filled out for each subject. This included name, age, birthdate, address, height, weight, chest measurement, and past history of illnesses and hospitalizations. Also important was a detailed statement of present habits, including daily exercise and competitive team sports both in school and in the home or community, intensity and frequency of bicycling, and smoking, television watching,

and sleeping habits. With this information we attempted to assess the person's physical fitness in order to test the correlation between physical activity and actual working capacity. Also we tried to differentiate factors which may contribute to optimal conditioning from those which decrease fitness.

Resting pulse rate and oral temperature were taken and recorded. Then the child was seated on the bicycle. For ideal mechanical advantage, the seat was adjusted so that the leg is in a position of nearly full extension when the pedal is at the lowest part of its excursion. Room temperature was kept at 70°F.

With the subject's mouth closed, expired air was sampled from either nostril by two plastic catheters which are connected to electronic devices for measuring percentages of nitrogen and carbon dioxide. Outputs from these two analyzers are fed into preamplifiers on a Sanborn direct-writing recorder. After calibration of the analyzers with standardized gases, a resting tracing was obtained of percent CO_2 and N_2 and of respiratory rate.

The first workload was set for the bicycle and the rider was instructed to begin pedalling slowly and to bring the tachometer needle up gradually to between 60 and 70 r.p.m. and to keep the speed within this range. The workload was kept constant until a steady state was reached. This usually required from two to five minutes. The steady state values

and sleeping habits. [illegible] to obtain the person's typical [illegible] in order to study the correlation between [illegible] and [illegible] ing capacity. Also we [illegible] may contribute to optimal conditions [illegible] creased fitness.

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for N_2, CO_2, respiratory rate and heart rate were recorded for one minute. The pulse rate was taken by radial palpation, by auscultation, or by electrocardiogram. Then the workload was increased and the process repeated until the anaerobic threshold was reached; this can be observed on the recording by the fall of the end-tidal nitrogen value below the inspired air baseline. After the subject stopped pedalling, oral temperature was again taken, as was the pulse rate after two minutes and five minutes of rest.

Two schedules of workload increase were used. In the first, the subject exercises at three different work levels at 100 kgm/min intervals for five to six minutes each. This schedule may be used to make certain a steady state has been reached, as well as to get a rough estimate of the anaerobic threshold. In the second, the subject pedals at six or seven different levels, which are 50 kgm/min apart, for two minutes each. This schedule is used to ascertain more precisely the anaerobic threshold.

Materials

Equipment for this study included the bicycle ergometer, analyzers with vacuum pumps for carbon dioxide and nitrogen, the Sanborn four-channel recorder, tanks of analyzed gas for precise calibration of the gas analyzers, and two high-gain DC preamplifiers for the Sanborn to receive outputs from the analyzers.

for N_2, O_2, respiratory rate and heart rate were recorded for one minute. The pulse rate was taken by radial palpation, by auscultation, or by electrocardiogram. Then the workload was increased and the process repeated until the anaerobic threshold was reached; this was characterised by the reaching [illegible] the fall of the [illegible] below the baseline [illegible]. Then the subject stopped pedalling, rectal temperature was again taken, as was the pulse rate after [illegible].

Two schedules of workload increase were used. In the first, the subject commenced [illegible] at 1000 [illegible]. This schedule was used to [illegible] reached, as well as to get a rough estimate of the anaerobic threshold. In the second, the workload [illegible] different levels [illegible] each. This schedule [illegible] anaerobic threshold.

Materials

Equipment for this study included the [illegible] analysis [illegible], the Sanborn four-channel [illegible] precise calibration of the gas analysers, [illegible] of [illegible] analysers.

The CO_2 analyzer is a Beckman/Spinco Model LB-1 Medical Gas Analyzer designed especially for physiological testing. The analyzer consists of two main units, a pickup and an amplifier, with a cable connecting them. The pickup unit (Fig. 3) detects the percent CO_2 from the expired air sample and gives off to the amplifier an electrical signal which is proportional to concentration. The amplifier then transforms this signal into a needle deflection on a meter and into an output which is fed into the recorder (46). The property of carbon dioxide of absorbing infrared radiation in proportion to concentration offers the fastest and simplest way of measuring the CO_2 concentration of alveolar air (46); this is used as the operating principle of the device.

After the gas sample reaches the sample cell, time required for CO_2 meter deflection to 90 percent of full scale is 0.1 sec. (46). The swift response time makes possible the immediate evaluation of each breath.

The CO_2 analyzer is calibrated with two pressurized tanks of previously analyzed dry gas which contain 4 percent and 7 percent CO_2 respectively, with a balance of nitrogen. The gas is delivered into a 25 inch plastic catheter which is connected to the pickup unit.

An expanded scale is used in order to appraise more accurately the percentages of CO_2 in the subject's expired air. The analyzer is accurate to 0.1 percent CO_2 at any concentration between 1 percent and 10 percent.

The CO_2 analyzer is a Beckman/Spinco Model LB-1 Medi-cal Gas Analyzer designed especially for physiological work-ing. The analyzer consists of two main units, a pickup unit and an amplifier, with a cable interconnecting them. The pickup unit (Fig. 7) converts the percent CO_2 from the incoming air sample and gives off to the amplifier an electrical signal which is proportional to concentration. The amplifier then trans-forms this signal into a meter deflection on a meter and into an output signal to the tape (or recorder use). The property of carbon dioxide of absorbing infrared radiation in proportion to concentration makes the reason and prac-tical way of measuring the CO_2 concentration of alveolar air (18). This is used as the operating principle of the device.

After the gas sample reaches the sample cell, time re-quired for CO_2 meter deflection to 90 percent of full scale is 0.1 sec. (18). The quick response time makes possible the immediate evaluation of each breath.

The CO_2 analyzer is calibrated with two precision-made tanks of previously analyzed gas mixtures containing 1 percent and 7 percent CO_2 respectively with a balance of nitrogen. The gas is delivered into a 27 inch capacity calibrator which is connected to the pickup unit.

An expanded scale is used in order to visualize more ac-curately the percentages of CO_2 in the end-tidal (alveolar) air. The scale is accurate to 0.1 percent CO_2 at any concen-tration between 1 percent and 10 percent.

For analysis of percent alveolar nitrogen a Nitralyzer Model 300 AR made by Med-Science Electronics was used. The pickup unit in which the gas sample is analyzed is connected to a vacuum pump which draws the gas through the system. A needle valve sampling mechanism lets the gas into an ionization chamber (16 ml/min). The ionized gas emits light which is then filtered so that the only region of the spectrum which passes the filter is that in the range of the intense nitrogen bands. A photocell detects the filtered light and sends a signal to the amplifier unit. This amplified signal then indicates percent nitrogen in the sample on a meter. The amplifier also sends an output to the Sanborn (47).

The operating pressure within the ionization chamber determines the shape of the calibration curve and the sensitivity of the Nitralyzer. When the pressure is low, small fluctuations in pressure may cause significant errors. The recommended pressure of 0.6 mm.Hg is low enough so that the calibration curve is fairly linear, but high enough so that small fluctuations have little effect. If the ionization current is kept between 0.5 mm.Hg and 0.8 mm.Hg, it has essentially no effect on the calibration curve (47).

The Nitralyzer is calibrated for each experiment with pressurized, previously analyzed gas tanks of 80.7 percent nitrogen with balance CO_2 (5%) and O_2 (14.3%), and of 78.5 percent nitrogen with balance CO_2 (5.2%) and O_2 (16.3%).

For analysis of percent nitrogen [illegible] Nitrala-zer Model 100 [illegible] made by [illegible] Incorporated was used. The [illegible] in which the gas sample is analyzed is connected to a vacuum pump which draws the gas through the system. A needle valve [illegible] into an ionization chamber [illegible]. The emitted light which [illegible] of the spectrum which [illegible] in the range of the [illegible] nitrogen bands. A photocell detects the filtered light and sends a signal to the amplifier and this amplified signal [illegible] of the sample on a meter. The amplifier also sends an output to the recorder (17).

The operating pressure within the [illegible] chamber determines the range of the [illegible] and the sensitivity of the [illegible]. When the pressure is [illegible], small fluctuations in pressure can cause [illegible]. The recommended pressure [illegible] when the calibration [illegible] small fluctuations have little effect. If the [illegible] current is kept between [illegible] essentially no effect on the [illegible] (17).

The Nitralyzer is calibrated for each experiment [illegible] preparations, previously analyzed [illegible] percent nitrogen with balance [illegible] and [illegible] percent nitrogen with balance [illegible] (14,20).

The calibration curve of the Nitralyzer was made with dry gases and is not correct for wet gases. Therefore, since the expired air to be measured is saturated with water, it is necessary to saturate the known mixtures before reading their values for the curve. This is done by bubbling the gases through a water trap system and then into the sampling catheter.

Water vapor also has an effect on the concentration of nitrogen in room air. It is found that saturating air with water causes an appreciable decrease in the nitrogen percentage. A subject's baseline for percent inspired nitrogen on the Sanborn conforms closely to the line obtained from sampling saturated room air. So, in order to get the value of air for the calibration curve, it is necessary to bubble compressed room air through the water trap.

An expanded scale of 10 percent of the full range is also used for nitrogen analysis. This particular range enables the analyzer to measure very sensitively small differences between a known gas and an unknown gas (47). Thus minute changes in alveolar nitrogen concentration can be monitored with great accuracy.

The Lode bicycle ergometer used in this study was designed by Lanooy to obviate some of the difficulties encountered with earlier ergometer models. All these had the disadvantage that changes in pedal r.p.m. caused changes in

loading, thus making it necessary for the rider to keep the r.p.m. constant (48).

A fundamental principle of the Lode ergometer is that the energy converted to heat (the product of distance per unit time and the braking power) remains constant in spite of changes in r.p.m. This principle involves a copper disk turning in an electromagnetic field. Where work done is A, force (in kg.) applied to the braking magnet is P, distance from the disk center to the point of application of braking force is r, and disk r.p.m. is n,

$$A = P.2 \quad (n/60) \text{ kg-m./sec.}$$

If A is not to vary with r.p.m., either P or r, or Pr must vary inversely with n. It was found that, within a certain range of speed, P will decrease hyperbolically when n increases, thus making the value for Pn constant (48).

By using a particular transmission ratio between pedals and disk the critical disk r.p.m. will be exceeded in spite of very low pedal r.p.m. (47).

For physiological reasons the designers supply a tachometer and urge indicating a speed to the subject. It is their opinion that tempo may influence such factors as mechanical efficiency (47). In this study, following the example of Adams (15,16), Cumming (14), and Bengtsson (13), we encouraged the subject to keep the pedal r.p.m. between 60 and 70.

loading, thus serving as necessary for the latter to keep the r.p.m. constant (14).

A fundamental principle of the ergometer is that the energy converted to heat (the product of distance per unit time and the braking power) remains constant in spite of changes in r.p.m. This principle involves a torque disk running in an electromagnetic field. If the force (in kgs) applied to the braking moment is F, distance from the disk center to the point of application of braking force is r, and disk r.p.m. is n,

$$A = F \cdot r \cdot (2\pi n) \ kg.m./sec.$$

If A is not to vary with n, F must vary inversely with n. It was found that within a certain range of speed, F will increase (decrease) when n decreases (increases), thus keeping the product Fn constant (15).

By using a particular frequency ... between ... and that the ... will be ... in spite of very low pedal r.p.m. (17).

For physiological research the instrument supply a ... meter ... indicating r.p.m. to the subject. It is their opinion that there may influence each subject as mechanical efficiency (47). In this study, following the example of Asmussen (3,10), Swegaard (41), and Bengtsson (11), we encouraged the subject to keep the pedal r.p.m. between 60 and 70.

Another feature of this instrument is that the amount of electrical energy desired can be continuously regulated by a single knob (48). This energy is read on a Watt scale and can be translated into kilogram meters per minute, a widely used work unit (1 Watt = 0.1019716 kgm/sec.).

The recorder used is a Sanborn four-channel direct-writing thermographic recorder, Model 964. This recorder used interchangeable plug-in preamplifiers to translate the signals for gas analysis. Outputs from the Nitralyzer and the CO_2 analyzer are fed into Sanborn High Gain Preamplifiers Model 350-2700. Sensitivities and attenuations are adjusted on these preamplifiers to afford wide distances on the recording paper between the standardized high and low gases; this makes possible greater accuracy in determining percent of gas in the expired air (49).

<u>Determination of R</u>

The equation used to determine respiratory quotient from CO_2 and N_2 concentrations is derived (Fig. 5) from the alveolar ventilation ratio (37) $\frac{\mathring{V}_{CO_2}}{\mathring{V}_{O_2}}$ where $\mathring{V}_{CO_2}$ is the carbon dioxide production in ml. per min. and $\mathring{V}_{O_2}$ is the oxygen consumption in ml. per min; and from the alveolar gas equations (37) $\mathring{V}_{CO_2} = \mathring{V}_A \cdot F_{A_{CO_2}}$ where $\mathring{V}_A$ is alveolar minute volume and $F_{A_{CO_2}}$ is percent CO_2 in alveolar air, and

Another feature of this instrument is that the amount of [illegible] and is [illegible] regulated by a [illegible] (11). Thus whether it [illegible] small [illegible] can be [illegible] per minute, a widely used work unit [illegible].

The recorder used is a [illegible] four-channel direct-writing [illegible] recorder, [illegible]. This recorder used interchangeable [illegible] the signals for gas analysis. [illegible] the CO_2 analyzer [illegible] preampli-fiers Model [illegible]. [illegible] adjusted [illegible] the [illegible] gases. [illegible] percent of gas [illegible].

Determination of [illegible]

The [illegible] from CO_2 and N_2 concentrations [illegible]. From the alveolar ventilation rate [illegible] where [illegible] is the [illegible]

[illegible] and [illegible] is the [illegible] consumption [illegible] and from the [illegible] equations [illegible] where [illegible] is [illegible] and [illegible] is [illegible] CO_2 in alveolar air, and

$$\mathring{V}_{O_2} = \mathring{V}_A \cdot F_{I_{O_2}} \cdot \frac{F_{AN_2}}{F_{IN_2}} - \mathring{V}_A \cdot F_{A_{O_2}}$$ where $F_{I_{O_2}}$ is percent O_2 in inspired air, F_{AN_2}/F_{IN_2} is a correction factor, and $F_{A_{O_2}}$ is percent O_2 in alveolar air. R may be estimated during exercise with a nomogram constructed from this equation.

The recorder tracings (see Fig.4) provide all the data necessary for calculation of the respiratory quotient at each exercise level. Alveolar CO_2 and N_2 concentrations in the steady state must be determined at each work level. Percent of gas is indicated by millimeters of deflection on the recorder paper. Before exercise begins, deflection values for the standardized gases are plotted against percent gas on graph paper. Semi-log paper is used for CO_2 since the analyzer meter is calibrated on a logarithmic scale. The Nitralyzer scale is linear.Points on the graph obtained for higher and lower standard gas concentrations are connected by a straight line. Percent end-tidal gas of a subject is then determined by measuring amount of deflection and reading percent gas on the standard line. A reasonably steady state must be reached for accurate appraisal of deflection produced by a particular gas concentration. End-tidal concentration is represented by the last part of the deflection before the stylus returns to the baseline. End-

tidal concentration is assumed to be the same as alveolar concentration.

Since the R equation was derived using a room air nitrogen value of 79.1 percent, the value found for room air by the Nitralyzer must be compared with this value on the standard nitrogen graph. This difference is then subtracted from each of the exercise end-tidal nitrogen concentrations which will be used to calculate R.

Values of R for each exercise level are then plotted against work load in kg-m/min. on linear graph paper (Fig. 6). The threshold of anaerobic metabolism (TAM) is indicated as the work load at which R rises most significantly. (We used TAM as an index of working capacity and tested the correlation of this threshold with the variables age, height, weight, body surface area, and physical fitness. See Section 3). TAM is usually found around a pulse rate of 120, assuming a maximal rate of about 170-180. The relationship between TAM and working capacity for various weights is shown in Fig. 7. The greater the weight, the greater is the difference between TAM and working capacity, using values for physical working capacity obtained by Adams and Cumming (14,15,16). Thus TAM increases with increase in weight, but not at the same rate as does working capacity.

blood concentration is assumed to be the same as alveolar concentration.

Since the [illegible] was measured using a three [illegible] alveolar value of [illegible], the value found for [illegible] air by the rebreathing method [illegible] value on the standard [illegible]. This difference is [illegible] combinations which will be used in [illegible].

Values of [illegible] for each [illegible] level are then plotted against work load in [illegible] (Fig. [illegible]). The threshold of anaerobic metabolism (TAM) is indicated as the work load at which [illegible] rapidly. The mean TAM [illegible] tested the correlation [illegible] with the variables age, height, weight, body surface area and [illegible] mass. (See Section [illegible]). [illegible] rate of [illegible]. The relationship [illegible] capacity for various weights is shown in Fig. [illegible]. The heavier the subject, the greater is the difference between TAM and [illegible] capacity using values for [illegible] by Adams and [illegible] ([illegible]). Thus TAM increases with increases in weight, but not at the same rate as does working capacity.

Admissibility of Data

There are some serious difficulties in obtaining reliable data with this method. Irregular breathing and hyperventilation are common problems which make it impossible to assess the real respiratory quotient. These irregularities can be observed on the tracings, and the data from these tracings is rejected. Criteria for admissibility of data thus include the attainment of a steady state at each exercise level for at least one minute, a regular breathing pattern, and the absence of hyperventilation at least in the sections of the tracing where the measurements are made.

Of the tracings obtained with normal subjects 54.5% were good tracings, 14.8% were good enough to estimate closely the RQ values, 24.6% were rejected because of hyperventilation, and 6.1% were rejected because of irregular breathing and failure to reach a steady state.

Section III - Results and Discussion

Results of Previous Studies in Children

There have been very few exercise studies in children done in the past, and these have involved, for the most part, measurement of the physical working capacity -- the workload at which a pulse rate of 170 per minute is attained.

In 1956 Bengtsson (13) evaluated working capacity in normal children on a bicycle ergometer and compared the results with those for normal adults. The children, aged 5 to 15, had very similar habits regarding games and sports. Each exercise load lasted about six minutes, and a steady state was assumed if heart rate at four and six minutes was within eight beats and respirations within six breaths of each other. Usually three loads were used to raise the heart rate to about 170 per minute.

Bengtsson found that working capacity in boys was somewhat higher than in girls, but the difference was not statistically significant. He concluded that there was no real sex difference. The working capacity increased rectilinearly with age in all the children. Standard deviations from the mean were large, however, mainly in the younger children. The author attributes this to differences in physical conditioning.

He found the most significant correlation to be with body weight. Working capacity has a higher coefficient of correlation with weight than with body surface area. Also, with the weight relation, the standard deviation is less. Children with similar working capacities were grouped in weight ranges -- 17-24 kg. (5-6 yrs.), 25-28 kg. (7-9 yrs.), 29-39 kg. (10-12 yrs.), and 40-60 kg. (13-14 yrs.)

In 1961 Adams et al. (15) studied 243 normal California school children aged six to 14. As in Bengtsson's study, the subjects rode a bicycle ergometer at three different work levels for six minutes at each load, reaching a pulse of about 170 at the last load. In boys the working capacity correlated well with log weight (correlation coefficient 0.81), log height (0.83), log surface area (0.81), and age (0.79). In the girls the working capacity correlated well with the same variables. These authors found a distinct sex difference (male working capacity greater than female) which was present at the early ages and then became more pronounced with increasing age.

Adams, Bengtsson, et al. (16) used the bicycle ergometer with two work loads to reach a pulse rate of 170 in 196 normal Swedish children aged 10 to 12. They attempted to evaluate the degree of physical fitness and used this as a variable. Working capacity increased with age, height,

He found [illegible] significant correlation [illegible] body weight. [illegible] of correlation with [illegible] Also, with [illegible] less. [illegible] grouped [illegible] (7-9 yrs.) [illegible] yrs.)

In 1961 Adams et al. [15] [illegible] school children [illegible] the subjects rode a [illegible] work levels for [illegible] minutes at each level [illegible] of about 170 [illegible] correlated well with [illegible] 0.83 [illegible] leg [illegible] (0.79). [illegible] with the same [illegible] difference [illegible] was [illegible] compared with [illegible]

A [illegible] meter [illegible] 199 normal [illegible] to evaluate [illegible] a bicycle [illegible]

weight, and body surface area. Height, weight and body surface area had the highest correlations in the country girls. For the city girls and country and city boys the best correlation was with heart volume. There was also a significant correlation of working capacity with physical fitness. The boys had greater working capacities than the girls for the same body size, age, and heart volume.

Cumming and Cumming (14) used the same method to study 112 Canadian children aged six to 16. For the boys working capacity correlated very well with height (.865), weight (.897), and surface area (.904). Correlation coefficients for the girls with the same variables were not so high. The authors considered the number of subjects in the study too small to permit evaluation of physical fitness as a determinant of working capacity. They speculate that perhaps those children who compete in athletics have innately high working capacities.

Kramer et al. (50) tested 24 girls and 77 boys with maximal exercise on a combination bicycle-treadmill. This group included trained athletes, normals, and children with various cardiac abnormalities. Subjects who pursued competitive athletics were found to have greater maximal oxygen consumption and greater working capacity than others of the same age, sex, and size. There was significant overlap in working capacity between normals and children with cardiac problems.

Thus, the children with cardiac difficulties could not always be differentiated from normals by this test.

Duffie and Adams (51) used graded submaximal exercise on a bicycle ergometer to evaluate children with congenital heart disease (including atrial and ventricular septal defects, aortic and pulmonic valve stenosis, aortic and mitral valve insufficiency, tetralogy of Fallot, coarctation of the aorta, etc.). The subjects pedalled at three levels, then the pulse was extrapolated to 170. Many were tested before and after corrective surgery. The results obtained were compared with those for normal children. The working capacities of the majority of the children with obstructive lesions fell around the 30th percentile for normal children of the same surface areas, although there was considerable spread. Patients with left-to-right shunts performed as a group in the 36th percentile, although the range was from the 5th to the 95th. The degree of impairment in this group seemed to depend on the degree of pulmonary hypertension. The mean for eleven cyanotic patients was the 15th percentile.

Of 24 children who had corrective surgery, some fifteen showed improvement ranging from five to 70 percentiles. Nine showed no change in working capacity or had lower ones ranging from five to 80 percentiles. (Three of these had pulmonary hypertension and a fourth developed atrio-ventricular block postoperatively).

Naimark et al. (37) studied 33 normal adults and ten patients on the bicycle ergometer and found increases in respiratory exchange ratio in the patients at lower work levels than for the normals with little overlapping. Wasserman and McIlroy (1) found numerous inconsistencies comparing symptoms and catheterization data with anaerobic thresholds in a bicycle study of 37 cardiac patients.

In summary, previous determinations in normal children of physical working capacity (signified by attaining a heart rate of 170) with the bicycle ergometer have shown significant correlations with age, height, weight, body surface area, and physical fitness. Children with severe cardiopulmonary disease fall below healthy children in working capacity, but significant overlapping is seen between normals and those with less severe problems. In adults studied by determination of the anaerobic threshold the data comparing healthy persons with persons with cardiac problems is conflicting.

<u>Results</u> (see Figs. 8 through 12)

TAM for each individual was plotted against age, height, weight, body surface area, and physical fitness. Regression lines were calculated for each relationship. Then the significance of the correlation between TAM and each of these measurements was evaluated by t-testing. The graphs show

obvious scatter for these relationships. Nevertheless, each correlation is found to be statistically significant.

The correlation between age and anaerobic threshold (TAM) for 32 normals is given by the linear regression line $Y = 124.6 + 10.8X$. The value of t for the 32 pairs is 2.454. Thus the correlation is significant at $p < 0.05$.

For body surface area and anaerobic threshold in 32 normals $Y = 249.97 + 1.11X$. T is 5.740 and the correlation is significant at $p < 0.01$.

For body weight and anaerobic threshold in 35 normals $Y = 115 + 2.8X$. T is 3.343 and the correlation is significant at $p < 0.01$.

For height and anaerobic threshold in 35 normals $Y = 2.4X - 118$. T is 2.884 and the correlation is significant at $p < 0.01$.

Thirty-eight normals were placed into one of three categories as they were appraised by their exercise and living habits to be relatively unfit, moderately fit or very fit. The first two groups were combined, then anaerobic thresholds of the two remaining groups were compared by t-testing to determine whether or not there was a significant difference in aerobic capacity between them. The value for t is 3.709, and the difference is significant at $p < 0.001$.

obvious reason for these relationships. Nevertheless, each correlation is found to be statistically significant.

The correlation between age and [illegible] (TAAP) for 18 animals is given by the linear regression line $Y = 124.6 - 0.40X$. The value of t for the 18 pairs is 2.45. Thus the correlation is significant at $p < 0.05$.

For body surface area and [illegible] for 18 animals [illegible] the formula [illegible] and the correlation is significant at $p < 0.05$.

For body weight and [illegible] for 18 animals $Y = 113$ [illegible]. t is 3.10 and the correlation is significant at $p < 0.01$.

For height and [illegible] for 18 animals $Y = 2.47$ [illegible]. t is 2.64 and the correlation is significant at $p < 0.05$.

Thirty-eight animals were divided into two [illegible] groups [illegible] to determine whether or not there was a significant difference [illegible]. The value for t is 3.77, and the difference is significant at $p < 0.01$.

Discussion of Results - Comparisons and Implications

Our results for normals are, for the most part, in agreement with those of previous exercise studies in children. We also find a significant correlation between threshold of anaerobic metabolism (analogous to physical working capacity in other studies) and each of the factors age, weight, height, and body surface area. The most significant factor in increasing cardiopulmonary capacity is found to be physical fitness.

As children grow their ability to do work increases in general. Allowing for normal variance and overlapping, older children are taller and heavier than younger ones. Age may bestow greater co-ordination on a child. Increased weight in proportion to height implies greater muscular strength. These variables are obviously important in determining a child's working capacity, especially due to the vast changes in size which occur as children grow.

On the other hand, the data gathered in this study suggest that factors other than age and size may be as important or even more so in strengthening cardiopulmonary function. These other influences pertain less to the predetermined genetic makeup of a child than to the flexible, individual life patterns which he may develop. Regardless of age or size, the subjects who took part in athletics most vigorously had the highest working capacities. Typically, a dedicated

eleven-year-old Little League baseball player who weighs 30 kg. will reach his anaerobic threshold after 100 kgm/min more work than a sedentary 17-year-old who weighs 74 kg. but smokes a package of cigarettes a day and takes only sporadic exercise.

It is clear that the effects of systematic training are profound. These effects mainly involve increasing the capacity for aerobic processes in the muscles. Åstrand et al. (52) showed that heart volume, stroke volume, and blood volume are larger in trained athletes than in sedentary people. Åstrand (53) compared championship skiers with normally active persons and found an average maximal oxygen intake of 80 ml/kg/min. for the skiers and 58.6 ml/kg/min. for the normals. These two groups had similar values for vital capacity, pulmonary ventilation, maximal heart rate and blood lactate concentration. Åstrand concluded from this study that a high aerobic capacity is an essential and distinguishing characteristic of persons with high endurance fitness.

Freedman et al. (54) found a rise in maximal O_2 consumption in athletes, with increases both in cardiac output and in arteriovenous oxygen difference. They also showed that training increases the maximum breathing capacity and the pulmonary arterial systolic, diastolic, and mean pressures. This pressure increase is thought to effect continued high left ventricle output with decreased filling time.

Gandevia (55) thinks that well-trained individuals may have a smaller ventilation requirement for a given amount of exercise than "normal" persons. Milic-Emilie et al. (56) demonstrated that at a given metabolic level the oxygen cost of respiration is less in trained subjects than in untrained ones. Therefore, for any given level of oxygen uptake, a trained person will have a larger percentage of the total O_2 uptake available to muscles other than the respiratory muscles.

Andrew et al. (57) found that training produced no change in stroke volume or oxygen consumption, a rise in arteriovenous O_2 difference, and a fall in heart rate, cardiac output, and ventilation per minute for a given load. They suggest that the circulatory consequences of training may involve more effective redistribution of the blood volume, with decreased cardiac output to the skin. They also speculate that in athletes an increased body core temperature with resultant increased diffusion rates of gases and metabolites may play a role in augmenting working capacity.

According to Asmussen (3), both exercise and inactivity may vastly affect the aerobic capacity. Regular training can increase the aerobic capacity to as high as 50 percent above the standards for normals of any particular age or size. On the other hand, the sedentary life can reduce this capacity to less than 50 percent of the standard values for normals.

Andersen (55) notes that well-trained individuals may have a smaller ventilation requirement for a given amount of exercise than untrained persons. Williams et al. (56) demonstrated that at a given metabolic level the oxygen cost of respiration is less in trained subjects than in untrained ones. Therefore, for any given level of oxygen uptake, a trained person will have a larger percentage of the total O_2 uptake available to muscles other than the respiratory muscles.

Lichtner et al. (57) found that training produced no change in stroke volume or oxygen consumption, a rise in arteriovenous O_2 difference, and a fall in heart rate, cardiac output, and ventilation per minute for a given load. They suggest that the circulatory improvement of training may involve more effective redistribution of the blood volume, with increased capillary supply to the cells. They also speculate that in addition to increased body fluid temperature with localized increased diffusion rates of gases and metabolites may play a role in augmenting working capacity.

According to Lancaster (1), both exercise and inactivity may readily affect the aerobic capacity. Endurance training can increase the aerobic capacity to as much as 20 percent above the standards for persons of any particular age or size. On the other hand, the sedentary life can reduce this capacity to less than 70 percent of the standard values (1) normals.

Some investigators argue that even disposition to train and to compete in sports is inherited. Shephard (58) thinks that an individual may tend to participate in athletics because of a greater inherent capacity for muscular exercise. There may be some substance to this view. The evidence is nevertheless strong that by regular conditioning a person may significantly increase his aerobic capacity, regardless of the nature of his genetic make-up.

The results of the cardiac patients in this series bear out the heterogeneity in working capacity induced by the various degrees of conditioning. Harris et al. (59) reported that in exercise patients with heart disease have a smaller rise in cardiac output than normals, a greater fall in the oxygen saturation of mixed venous blood, an excessive increase in ventilation, and a higher oxygen debt and blood lactic acid concentration. Yet anaerobic thresholds for our cardiac patients overlap consistently with those of the normals. We find that a child with a ventricular septal defect or aortic stenosis may do as well as or better than a healthy individual of the same age or weight. The patients who lead active lives will often have relatively high anaerobic thresholds, clinical and catheterization data notwithstanding.

Assessment of the Method -- Problems and Possibilities

During this study we have encountered some serious problems in applying the chosen method. Thirty percent of the tracings have been entirely worthless as sources of data and have had to be discarded.

In the first place we must remind ourselves of the persistent difficulties of assessing true alveolar gas concentrations even with a normal breathing pattern. In the R equation we assume that end-tidal gas concentrations equal alveolar gas concentrations. However, several factors have been cited (60) as possibly causing a non-ideal system in this respect. These include: 1) non-uniform velocity gradients across a section of a conducting tube causing the central portion of the stream to outstrip those nearer the walls; 2) fore and back mixing due to acceleration and deceleration eddies which occur in inspiration and expiration; 3) non-uniform velocity gradients due to expansions, contractions, and bends in the conducting tubes; and 4) non-simultaneous emptying of all parts of the "mixer" into the conduction system.

In addition, there are common instances of irregular breathing patterns which reduce the reliability of the data. The most persistent problem is that of hyperventilation, causing a high rise in respiratory exchange ratio and making it impossible to determine the presence or absence of metabolic acidosis. This contrasts sharply with the earlier re-

Assessment of the Method -- Problems and Possibilities

During this study we have encountered several serious problems in applying the above method. Thirty percent of the tracings have been entirely worthless for analytical data and have had to be discarded.

In the first place we must remind ourselves of the mathematical difficulties of insertion true alveolar gas concentrations with a normal breathing pattern. In the [illegible] equation we assume that end-tidal gas concentrations equal alveolar gas concentrations. However, several factors have been cited (40) as possibly causing a deviation in this respect. These include: 1) non-uniform velocity gradients across a section of a conducting tube causing the central portion of the stream to [illegible] between the walls; 2) lack of [illegible] mixing due to ventilation and the deleterious gases which occur in inspiration and expiration; 3) non-uniform velocity gradients due to [illegible] constrictions and bends in the conducting tubes; and 4) non-simultaneous emptying of all parts of the alveolar area into the conducting system.

In addition, there are several limitations of irregular breathing patterns which reduce the reliability of the data. The most important problem is that of hyperventilation causing a high value in respiratory exchange ratio and making it impossible to determine the presence or absence of metabolic acidosis. This corresponds exactly with the earlier re-

ports of Wasserman and McIlroy (37,1) that hyperventilation presented no problem in their studies.

It is well known that anticipation of effort produces certain psychic stimuli which prepare the body for exercise. Hueting (61) studied eight non-trained subjects in ergometric exercise and found in the last minute of rest before work significant increases in heart rate, respiratory minute volume, and oxygen consumption. It is likely that the environment of tubes and electronic machines and the awareness of a test situation produce some physiological changes such as these.

In order for respiratory exchange ratio to equal metabolic respiratory quotient, the CO_2 stores (about 120 L in blood, soft tissues, and bone) must remain constant (3). A 50-percent increase in ventilation over one hour will eliminate 1.5 to 2.5 liters of CO_2. Respiratory exchange ratio will rise immediately to about 1.1 and will remain above 1.0 for at least ten minutes (62). Hyperventilation thus makes impossible the accurate determination of CO_2 production.

In our experience a hyperventilation pattern at rest and at light exercise will often disappear with a higher work level. This pattern is obvious on the tracing, and, should it persist past the first level or so, the tracing is discarded. Hyperventilation is denoted mainly by very low values for percent nitrogen, so that R may be 1.2 or higher even at rest.

The second major problem in obtaining a good determination of anaerobic threshold is irregular breathing. This may take any one of several forms, including cyclical hyperventilation and hypoventilation, grossly irregular respiratory frequency, and irregular depth of breathing with frequent sighing. These all tend to prevent attainment of a steady state. In some cases a second test re--duces or obviates the irregular breathing so that reliable data can be recorded.

It is possible that refinements may be made in this method so that more of the tracings will be acceptable. We have had some success in correcting irregular respiration and hyperventilation by distracting the subject's attention in various ways. At this time, however, the method remains limited in its usefulness because of the difficulty of reaching a true steady state in many individuals.

We have seen that normal children of the same age and size may have widely different anaerobic thresholds. For this reason it is difficult to establish standards for different ages and sizes. The best course is perhaps to try to obtain standard ranges of age groups (e.g. 2 or 3 years) and weight ranges.

Asymptomatic cardiac patients may also vary widely in anaerobic threshold and often have high aerobic capacity. Therefore, in our opinion, this method of screening these individuals will pick up only those with grossly low capaci-

The second major problem is obtaining a good determination of ventilatory capability in irregular breathing. This may take the form of [illegible] tidal volume, including hyperventilation and hypoventilation, erratic irregular respiratory frequency and irregular cycle of breathing with frequent sighs. These all lead to improper attainment of a steady state. In some cases a [illegible] or obviates the irregular breathing so that satisfactory data can be recorded.

It is possible that [illegible] may be [illegible] method so that more of the testing [illegible] by [illegible]. We have had some success in correcting irregular respiration and hyperventilation by instructing the patient [illegible] in [illegible] ways. At this time, however, the method remains limited in its usefulness because of the difficulty of reaching a true steady state in many individuals.

We have seen that normal individuals of the same age and size may have widely different ventilatory capacities. For this reason it is difficult to establish [illegible] for different ages and sizes. The best method of [illegible] is to obtain standard values of the [illegible] for a given age and weight range.

[illegible] patients [illegible] in [illegible] and [illegible] capacity. Therefore, in our [illegible] of [illegible] individuals with [illegible] with greatly low capacity.

ties. On the other hand, this method appears to be highly useful for evaluating the functional significance of a particular cardiopulmonary problem. A child's fitness to participate in all of life's activities can be assessed fairly accurately by determining his total cardiopulmonary function.

Also, the significance of a heart murmur or other problem can be evaluated over a period of time. If a child is forbidden to be active because of suspicion of disease, his aerobic capacity will decline markedly. If the problem is of little significance, the aerobic capacity will rise steadily with prescribed exercise. If, however, the problem is more serious, the anaerobic threshold will rise less or not at all. Thus, ability to change markedly the working capacity implies the cardiopulmonary flexibility inherent in a normal person. Inability to alter the anaerobic threshold under the stimulus of training implies physiological rigidity resulting from disease or congenital malformation. These changes with exercise will be easily discerned by testing on the bicycle at suitable intervals. Perhaps a training program using the bicycle itself might be devised.

Summary

In this study we have sought to utilize a simple and reliable method of evaluating total cardiopulmonary function in children which could be used for cardiac patients as well as for normals. The physiology of exercise was reviewed, and the specific metabolic basis for the chosen method was considered. This involves calculating respiratory exchange ratio from analysis of percent end-tidal N_2 and CO_2 in expired air. The workload at which R rises significantly represents the anaerobic threshold and is attained at a submaximal workload.

Subjects exercised on a bicycle ergometer; expired air was analyzed by electronic gas analyzers and percent gas registered on a Sanborn recorder. Threshold of anaerobic metabolism for each subject was calculated from the tracings, and this value plotted against age, height, weight, body surface area, and physical fitness. T-testing showed significant correlations for these relationships in normals. Physical fitness correlates well with TAM for any age or weight. TAM's for cardiac patients were not significantly below those for normals.

Frequent unphysiological breathing patterns limit the usefulness of the method. With it one can ferret out cardiac problems only if working capacity is very low (implying significant disease). This method is very useful for

evaluating a particular child's cardiorespiratory capacity, whether impaired or not, and for following its evolution over a period of time.

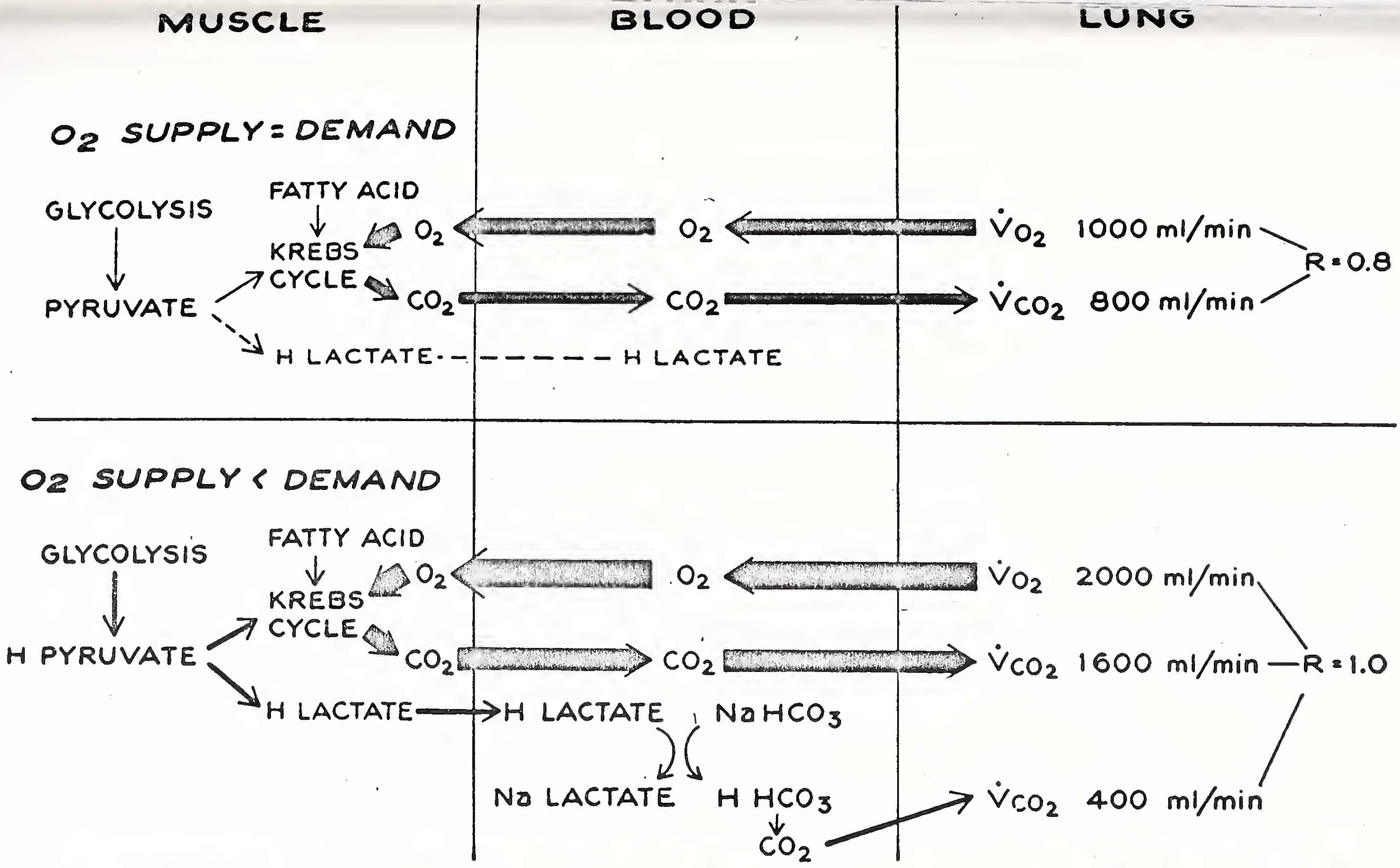
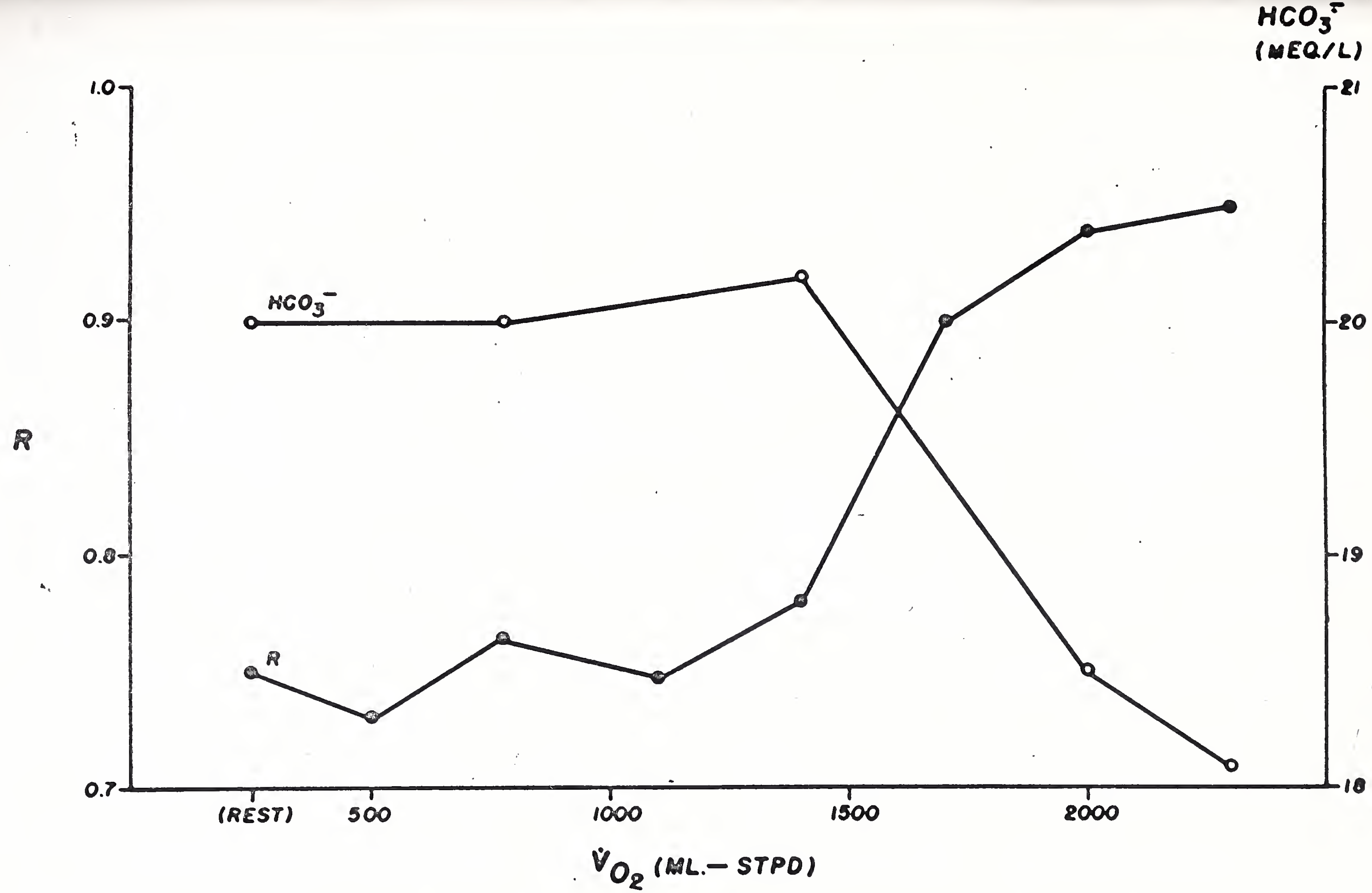


Figure I. Schematic representation of the relationship between R and metabolism during exercise. From Naimark (370)



CHANGES IN BICARBONATE AND RESPIRATORY QUOTIENT
WITH INCREASING WORK. FROM WASSERMAN (I)

In the pickup unit, beams from two infrared sources pass through the sample cell and the reference cell before entering the detection chamber (Fig. 3). The purpose of the reference cell is to provide equal intensities of infrared radiation to the two parts of the detection chamber when there is no sample.

The detection chamber is divided by a movable diaphragm into two compartments which contain equal and unchanging concentrations of the gas being analyzed. Infrared rays cause the gas molecules to vibrate more rapidly, thus bringing about an increase in pressure. When there is no gas sample present, this pressure rise is equal on both sides of the diaphragm. The concentration of gas in the detection chamber is less than one atmosphere. Since the pressure is relatively small, slight changes will be more significant than with a high pressure (46).

When the gas from outside reaches the sample cell, it absorbs a part of the infrared rays passing through the cell. This reduces the pressure in that side of the detection chamber by removing some of the radiation stimulus. The diaphragm bows out toward this side and thus alters the capacitance of the oscillator circuit. The result is a 60-cycle pulse; average amplitude of the 60-cycle peaks indicates CO_2 concentration. The amplifier in turn rectifies, phase demodulates, and rectifies this signal to produce the output (46).

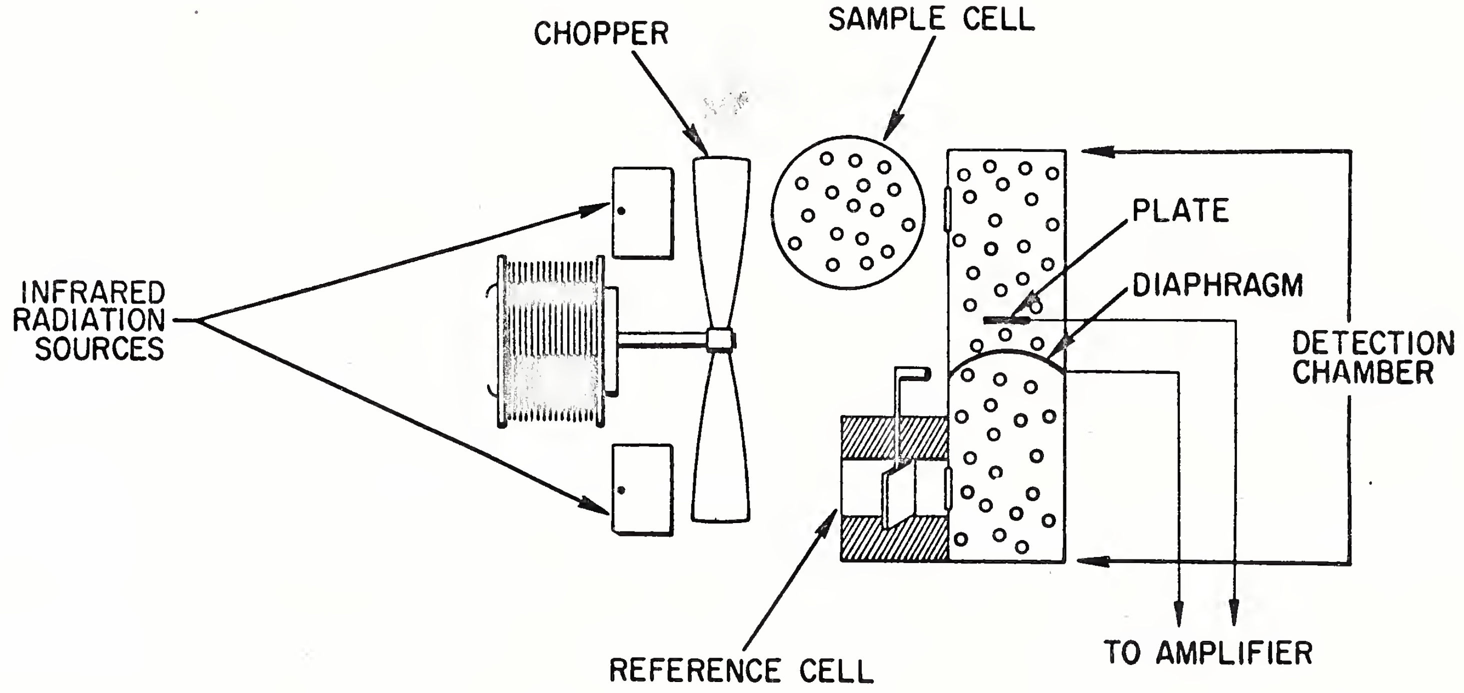


Figure 3. PICTORIAL DIAGRAM OF LB-1 PICKUP UNIT

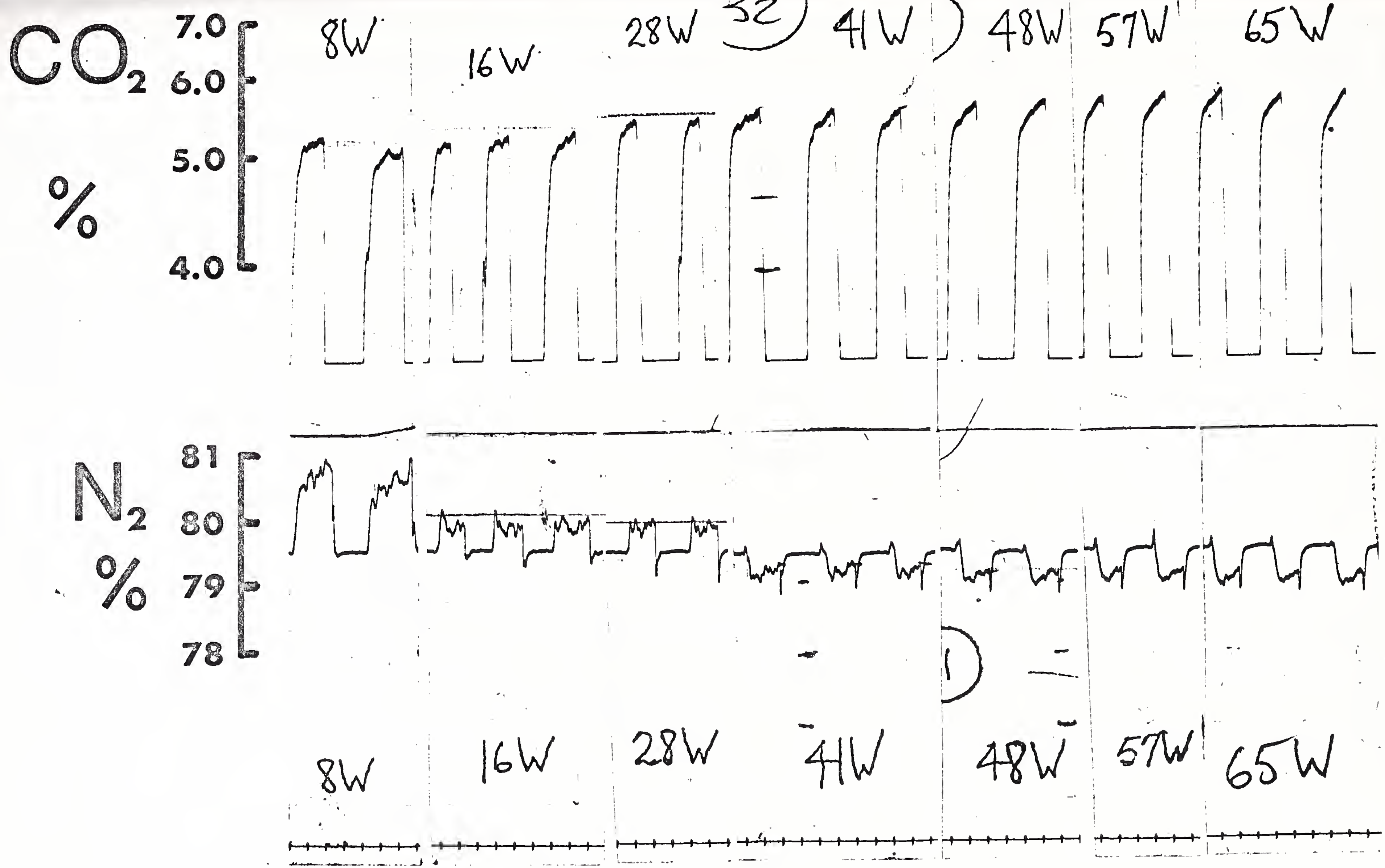


Figure 4. EXAMPLE OF SANBORN TRACING SHOWING RISE IN PERCENT CO_2 AND FALL IN PERCENT N_2 WITH INCREASING WORKLOAD(IN WATTS)

Figure 5

DERIVATION OF R EQUATION

$$R = \frac{\mathring{V}_{CO_2}}{\mathring{V}_{O_2}}$$

$$\mathring{V}_{CO_2} = \mathring{V}_A \cdot F_{A_{CO_2}}$$

$$\mathring{V}_{O_2} = \mathring{V}_A \cdot F_{I_{O_2}} \cdot \frac{F_{A_{N_2}}}{F_{I_{N_2}}} - \mathring{V}_A \cdot F_{A_{O_2}}$$

$$R = \frac{\mathring{V}_A \cdot F_{A_{CO_2}}}{\mathring{V}_A \left(F_{I_{O_2}} \cdot \frac{F_{A_{N_2}}}{F_{I_{N_2}}} - F_{A_{O_2}} \right)}$$

$$F_{I_{N_2}} = 0.791$$

$$F_{A_{O_2}} = 1 - F_{A_{CO_2}} - F_{A_{N_2}}$$

$$F_{I_{O_2}} = 0.209$$

$$R = \frac{F_{A_{CO_2}}}{1.26\, F_{A_{N_2}} - 1 + F_{A_{CO_2}}}$$

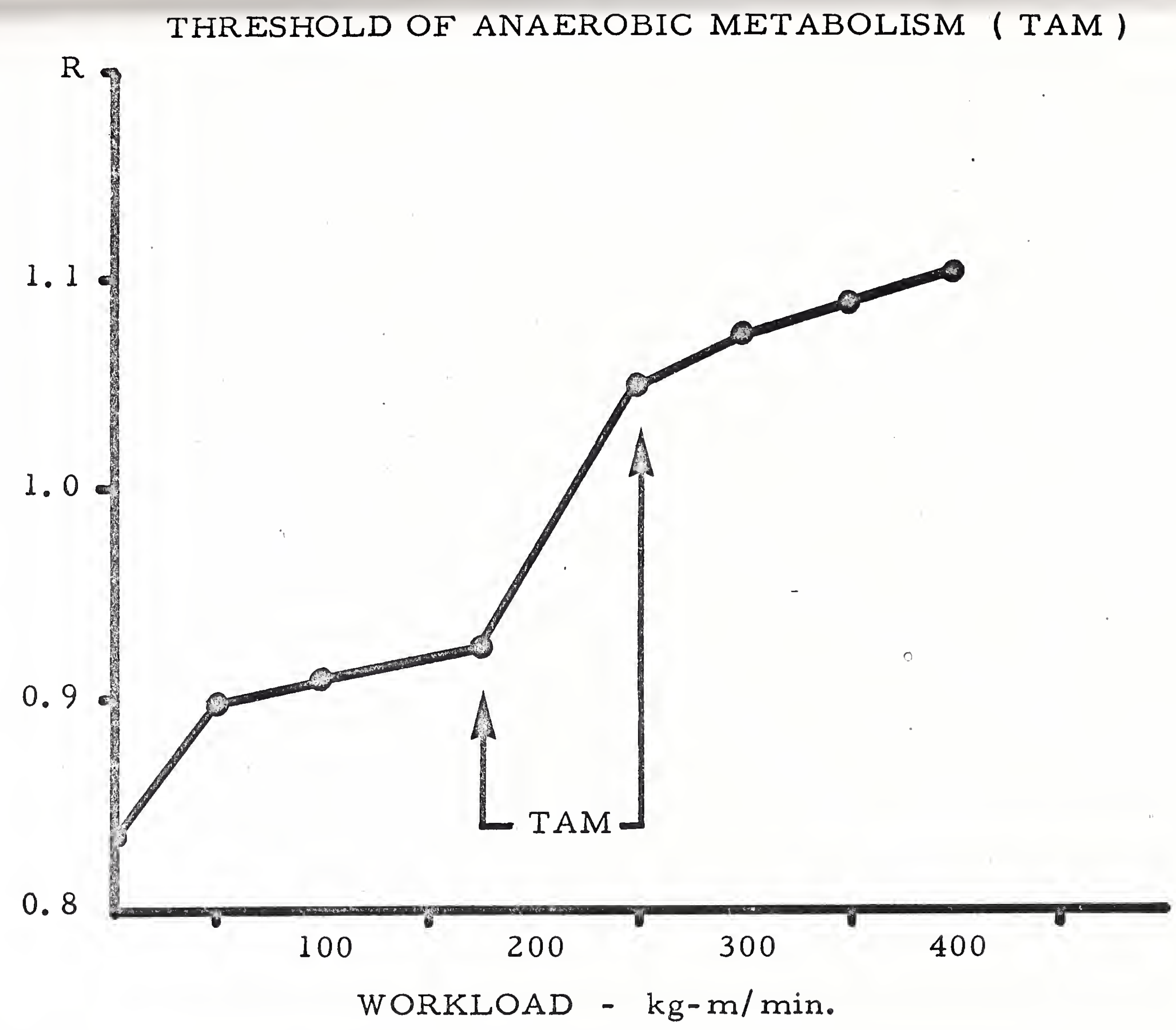


Figure 6. EXAMPLE OF R CURVE SHOWING ANAEROBIC THRESHOLD. VALUES TAKEN FROM TRACING IN FIGURE 4

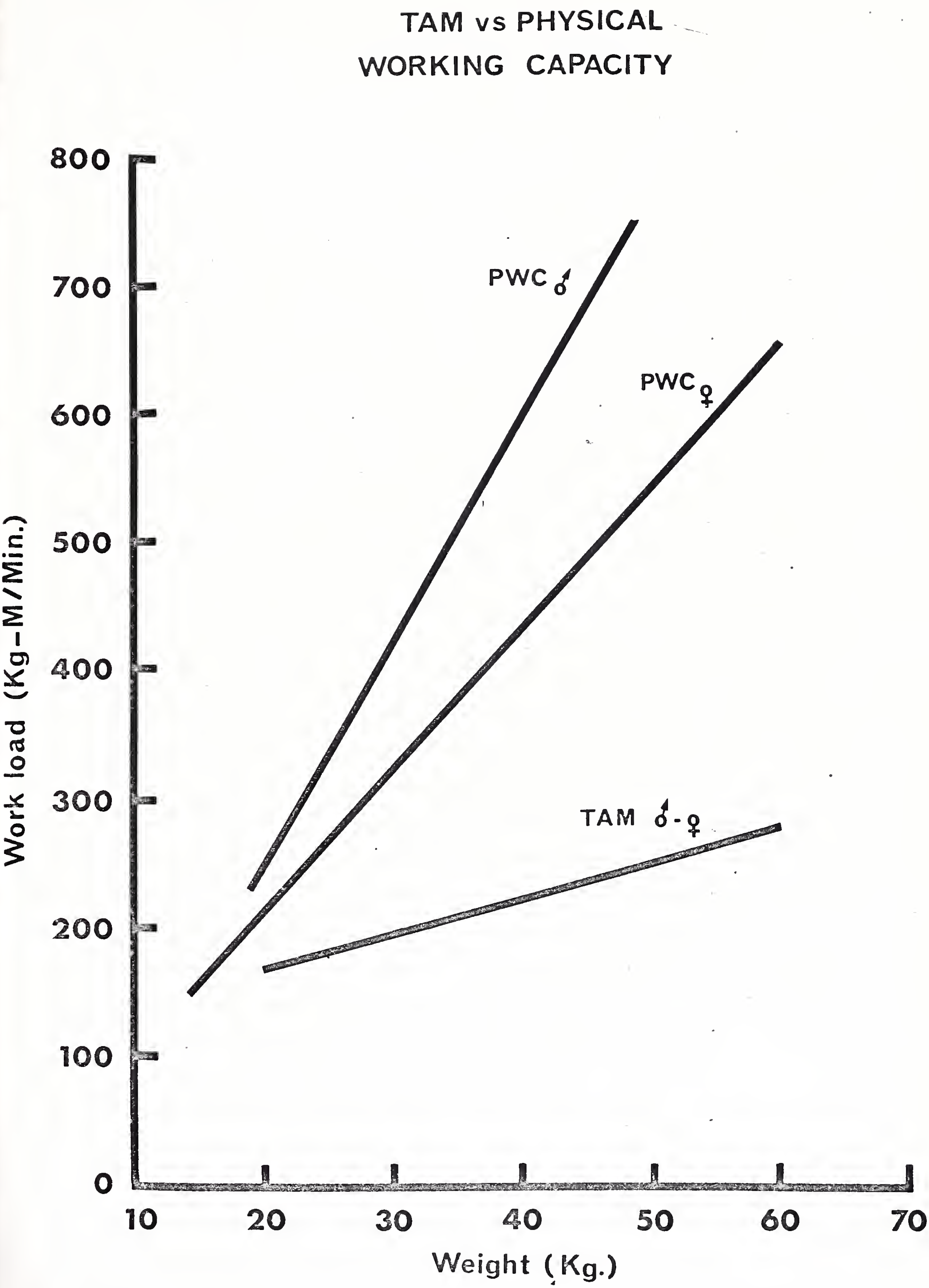

TAM vs PHYSICAL
WORKING CAPACITY
800
700
600
500
400
300
200
100
0
Work load (Kg-M/Min.)
PWC ♂
PWC ♀
TAM ♂-♀
10
20
30
40
50
60
70
Weight (Kg.)

Figure 7

TAM vs AGE IN NORMALS

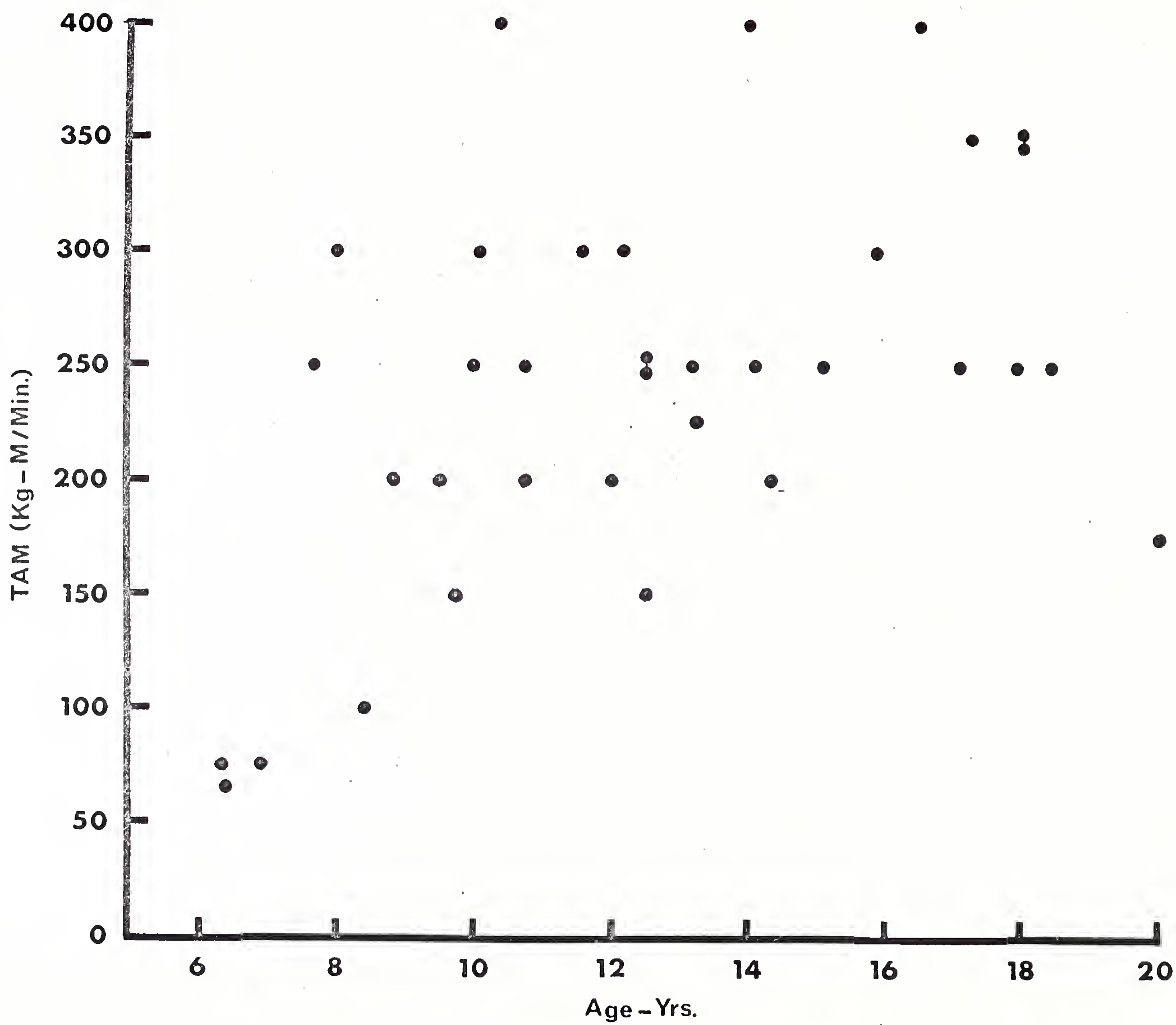


Figure 8

TAM vs BSA IN NORMALS

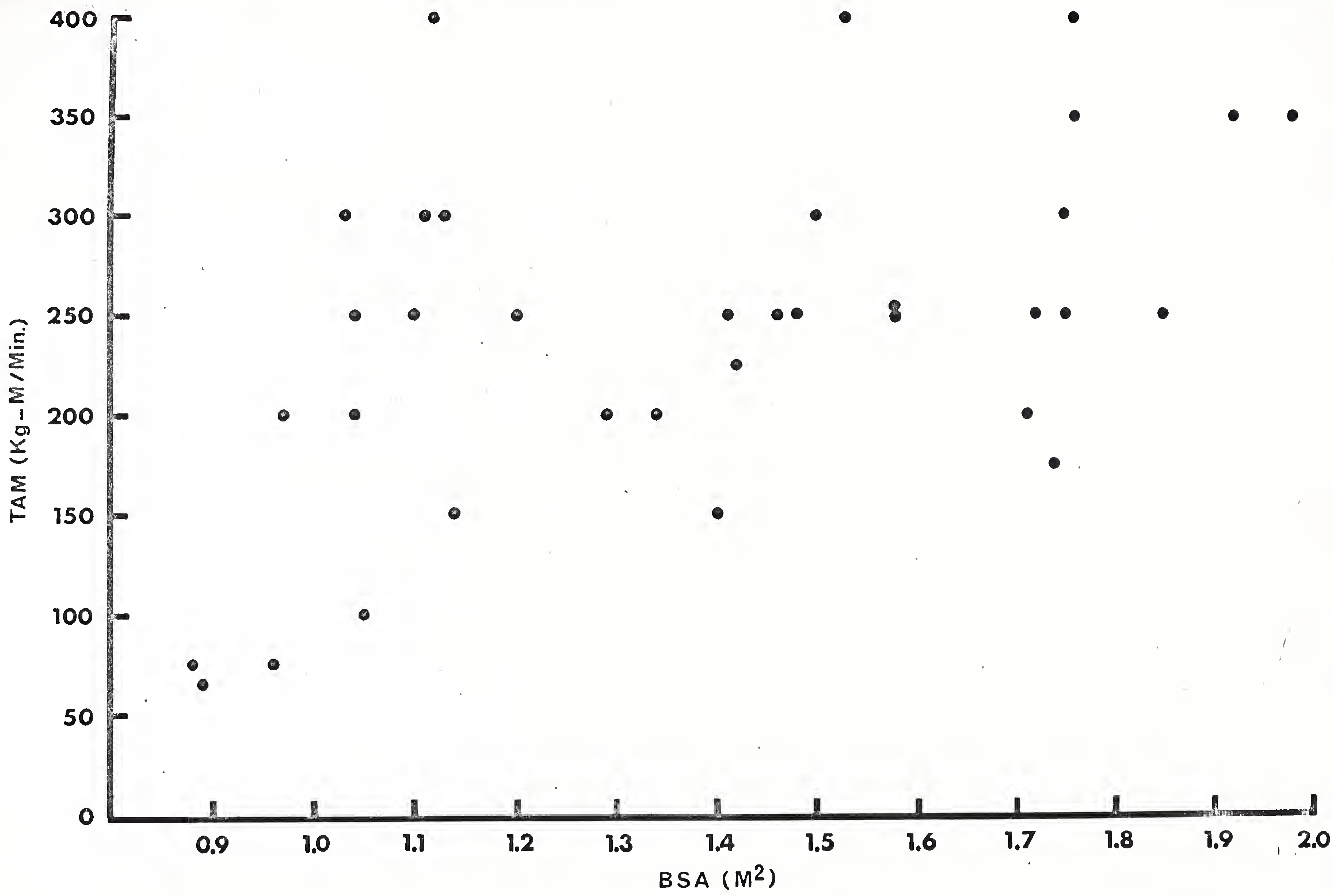


Figure 9

TAM IN NORMALS • AND IN CARDIAC PATIENTS o

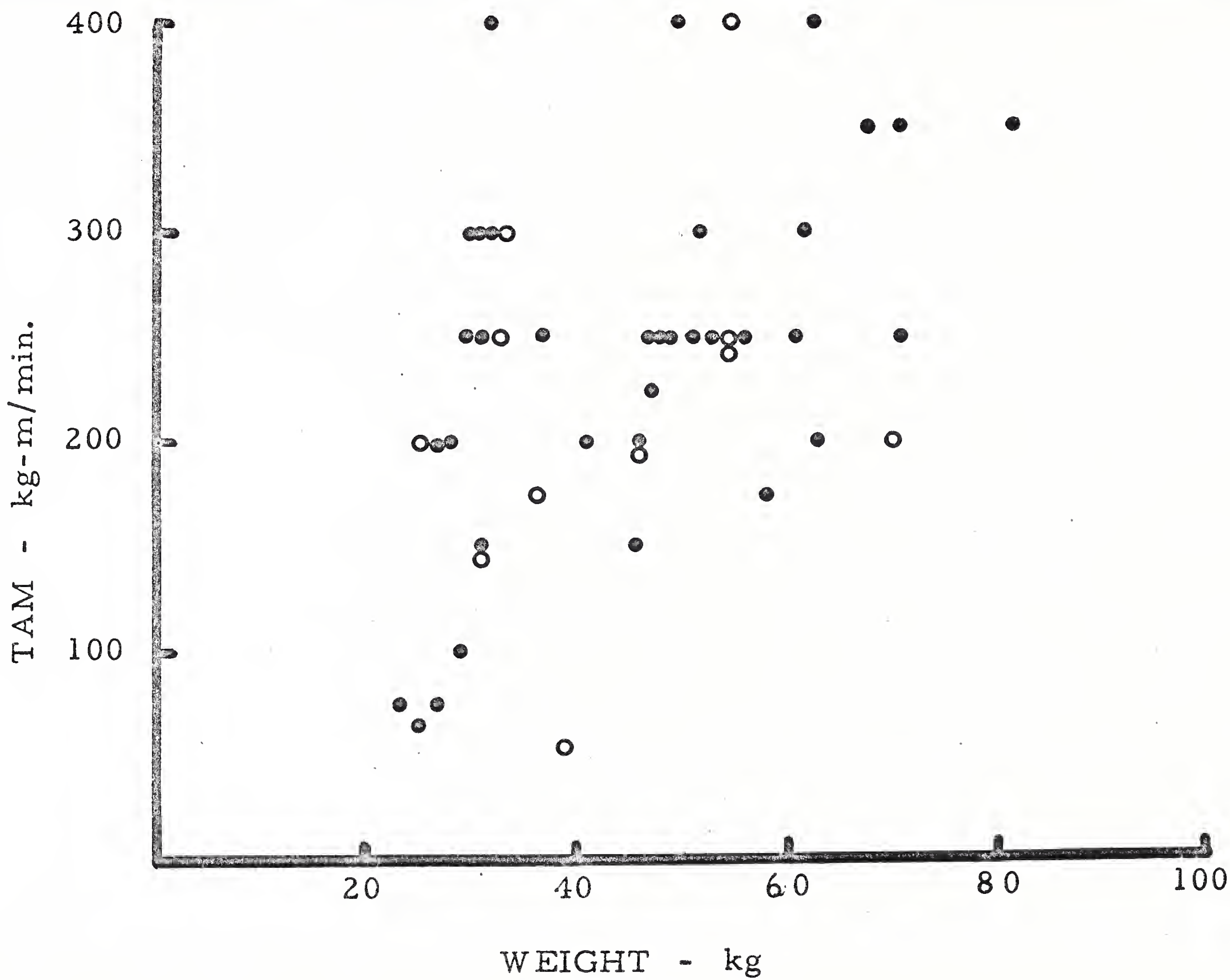


Figure 10

TAM vs HEIGHT IN NORMALS

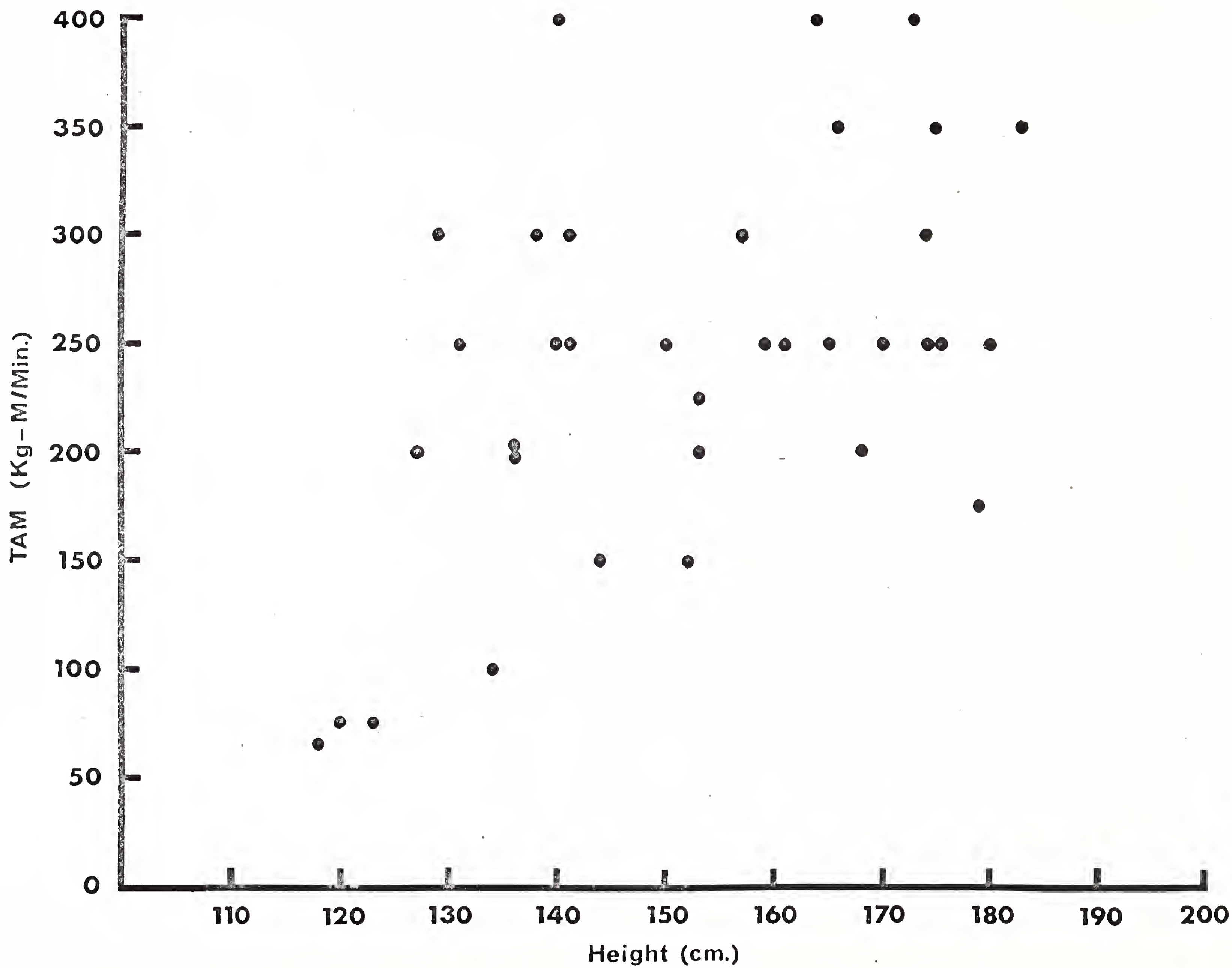


Figure 11

TAM vs. PHYSICAL FITNESS

IN NORMALS

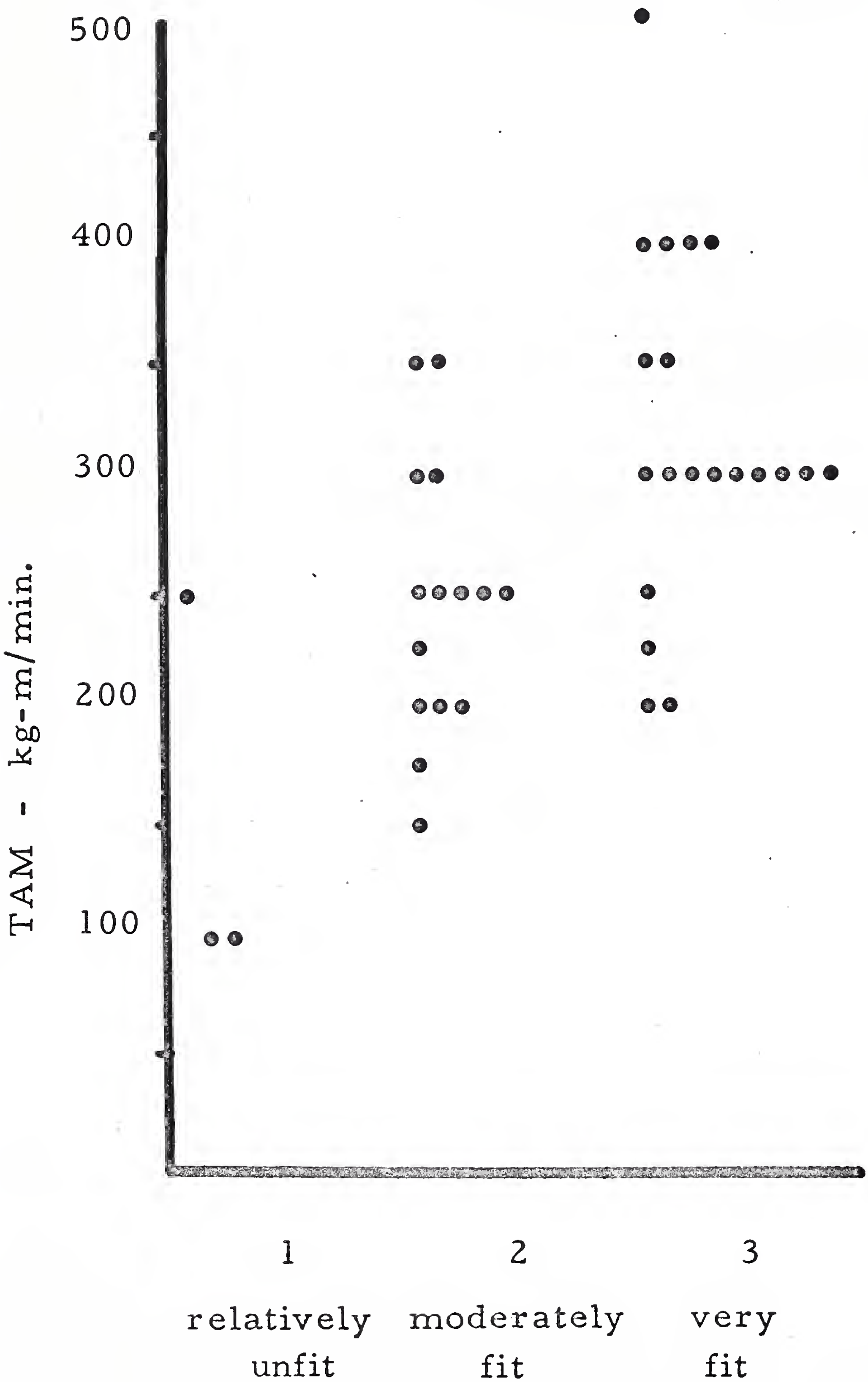


Figure 12

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